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THE CONTRIBUTION OF DRINKING WATER TO MINERAL NUTRITION IN HUMANS

Prepared for the
Environmental Protection Agency

by the

Nutrition Subcommittee
Safe Drinking Water Committee

Board on Toxicology and Environmental Health Hazards
Assembly of Life Sciences, National Research Council

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16. ABSTRACT

The first undertaking of the Safe Drinking Water Committee of the National Academy of Sciences was the identification of substances and their concentrations in the nation's water supply that might pose risks to the public health. This report, on the other hand, identifies and discusses substances found in drinking water which may have nutritional significance. The substances addressed include calcium, magnesium, phosphorus, fluoride, sodium, potassium, chloride, iodine, iron, copper, zinc, selenium, manganese, arsenic, nickel, vanadium, silicon, molybdenum, and chromium. For each substance, data on occurrence in food and water are reviewed, nutritional requirements, toxicity versus essential levels, and the contribution from drinking water are assessed. Recommendations are made regarding the appropriateness of controlling these substances in drinking water.

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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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THE CONTRIBUTION OF DRINKING WATER TO MINERAL NUTRITION IN HUMANS

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THE CONTRIBUTION OF DRINKING WATER
TO MINERAL NUTRITION IN HUMANS

GENERAL CONSIDERATIONS OF MINERAL INTAKE FROM WATER

The first undertaking of the Safe Drinking Water Committee (SDWC) was the identification of substances and their concentrations in the nation's water supply that might pose risks to the public health and, therefore, require the setting of limits. The committee's report, Drinking Water and Health (NAS, 1977) contained gaps where data were not available or were just emerging at the time the report was written. In other cases, data were not reviewed in depth because the specific substances were not considered pertinent to the initial charge of the committee, i.e., identification of adverse consequences of various substances in water.

One such area was that of nutrients, known to be essential or strongly suspected as being necessary for optimal health of humans and animals. While a few of the nutrients, notably the trace elements, were reviewed in the first report, the coverage was generally toxicological. The committee examined them as sources of potential risk to human populations.

In view of these considerations, the reconstituted Safe Drinking Water Committee established a Subcommittee on Nutrition and charged it with the responsibility of reviewing this area by selecting elements of interest and evaluating the effects of their presence in water. In this report, the subcommittee has examined the concentrations of nutrients in drinking water and the contribution of these concentrations to the observed intake and optimal nutrient requirements of human populations. It studied the benefits of the presence of an element in water and, in cases for which symptoms of both deficiency and toxicity are known to occur, adverse effects. This is a departure from most of the studies of the SDWC conducted previously or in progress, which were or are limited to adverse effects. The subcommittee chose to title this review The Contribution of Drinking Water to Mineral Nutrition in Humans, focusing on the positive effects of suites of elements that are known or assumed to interact in the environment or in biologic systems.

In Drinking Water and Health (NAS, 1977), the committee reviewed eight metals (chromium, cobalt, copper, magnesium, manganese, molybdenum, tin, and zinc) that are essential to human nutrition. The nutritional aspects of others, such as nickel, selenium, arsenic, and vanadium, were not considered. Rather, their toxicity was reviewed. In this study the subcommittee has reviewed potassium, chloride, iron, calcium, phosphorus, and silicon, and has extended the original review only where there was a need for updating or for examining a particular element as a nutrient as opposed to a potentially toxic substance. In the section on fluoride, the subcommittee decided against including an in-depth review because of its uncertainty concerning fluoride's essentiality to nutrition. However, in view of the contribution of fluoride to overall dental health and, through this, its effect on total health, some discussion of fluoride has been included in this review.

In this review chromium has not been dealt with at great length because it is not certain that the nutritionally useful form of the element occurs in water. It is generally thought that cobalt has nutritional value only as a component of vitamin B_{12}. Although some preliminary studies suggest that inorganic cobalt may have a physiological role independent of its functon in vitamin B_{12} (Raginski and Mertz, 1977), cobalt has not been discussed in this review.

The subcomittee has also examined the difference in water intake between young and adult humans. Infants (7 kg) consume approximately one-third as much water on the average as an adult, but their body weight is only approximately one-tenth of adult weight and the food intake is also obviously lower. For this reason, the water intake of an infant may contribute a significant quantity of a given element (NAS, 1974).

When people consume unusual diets, e.g., the diets of vegans, who consume no animal foods or dairy products, the intake of certain elements may be significantly different than the average. Athletes or people engaged in heavy labor and those living in a hot climate consume larger than normal amounts of water. In these instances, the contribution of water to the overall nutrient intake may be significantly different from the average.

The contributions from air have been considered only when amounts of possible significance were suspected. Where such contributions were negligible, no comment has been made. Only in rare instances, such as unusually high airborne levels, might air contribute to the nutrient needs of individuals. It is not always known whether elements taken in from such exposures are used for nutritional (metabolic) purposes.

Requirements for nutrients are generally discussed in terms of the recommended dietary allowances (RDA's) (NAS, 1974) or those intakes which have been judged adequate and safe (NAS, in press) not minimal intakes necessary for survival.

The subcommittee examined the new literature on water hardness because it involves nutritionally essential elements. However, it found no significant conclusive data concerning the relationship of water hardness and the incidence of cardiovascular disease since Drinking Water and Health (NAS, 1977) was published. An extensive evaluation of the literature in this area has recently been published

(NAS, 1979). Therefore, this topic is not covered in this report.

Clearly, some elements that have been reviewed are subject to changes in concentration in water because of the activities of humans. Elements in this category are zinc, copper, molybdenum, tin, manganese, nickel, and vanadium. These may require somewhat closer surveillance than elements such as magnesium whose concentrations in water appear to be affected very little by human activity.

The subcommittee believes that a study of the contribution of drinking water to mineral nutrition in humans is essential in a balanced appraisal of drinking water. It also believes that the data in this review are up-to-date and accurate and that they should help those charged with evaluating the nutritional value of drinking water in the United States.

Most information on the mineral composition of water has been gathered from large water-supply systems. In 1975, approximately 35.7 million water consumers (16.7% of the population) were served by systems supplying less than 25 persons. The minerals in water from smaller systems and individual supplies, e.g., wells, may exceed the concentrations in large water supplies, which form the basis for most levels cited in this report. Therefore, the potential contributions of water to nutrient intake that are given below must not be taken as the absolute limits.

The interplay between mineral elements and nutrition is exceedingly complex. In this report, it has been considered in light of the best available knowledge, but it should be remembered that this knowledge is still incomplete.

CALCIUM

Presence in Food and Water

Dairy products provide the largest source of calcium in the American diet. Table 1 lists calcium concentrations for some of these products and other foods (Davidson et al., 1975a).

In a survey of U.S. surface waters from 1957 to 1969, calcium levels ranged from 11.0 to 173.0 mg/l (mean, 57.1 mg/l) for 510 determinations (NAS, 1977). Finished water that was sampled in public water supplies for the 100 largest cities in the United States contained almost as much calcium (range, 1 to 145 mg/l). The calcium concentrations in 93% of the city supplies were less than 50 mg/l (Durfor and Becker, 1964). Similar results were reported in a Canadian study (Neri et al., 1977). Zoeteman and Brinkman (1977) reported that the public water supplies for 21 large European cities contained between 7 and 140 mg/l (mean, 85 mg/l).

The daily intake of calcium for most Western adult populations averages between 500 and 1,000 mg (Walker, 1972). The U.S. Health and Nutrition Examination Survey estimated calcium intakes for 20,749 people from 1 to 74 years old, and concluded that the only population segment with an intake appreciably (30%-40%) below the recommended daily allowance was the adult black female. The allowance values used in this survey were 450 mg for children aged 1

TABLE 1

Calcium Concentrations in Foods and Foodstuffs[a]

Food Item	Calcium Concentration, mg/100 g or 100 ml
Cheese, hard	500-1,200
Cheese, soft	80-725
Milk, cow	120
Milk, human	20-40
Nutmeats	13-250
Legumes, dried	40-200
Vegetables, leafy	25-250
Vegetables, roots	20-100
Grains, whole	4-60
Eggs	50-60
Fish	17-100
Sardines, whole	400
Meats	3-24
Fruits	3-60

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[a] Data from Davidson *et al.*, 1975a.

to 9 years, 650 mg for ages 10 to 16 years, 550 mg for 17 to 19 years, 400 mg for men 20 years and older, 600 mg for women 20 years or older, 800 mg for pregnant women, and 1,100 mg for lactating women (Abraham _et_ _al_., 1977).

Requirements

The amount of calcium required by the body daily and the level of dietary calcium needed to meet this requirement are controversial issues. Healthy individuals accustomed to low calcium diets appear to do as well as similar individuals accustomed to high calcium intakes. To some extent, the daily calcium allowances recommended by various international agencies reflect the calcium levels of normal local diets. In the United States, the Food and Nutrition Board of the National Research Council (NAS, 1974b) has recommended daily calcium intakes of 800 mg/day for adults on the basis that the daily excretion of calcium is 320 mg and that only 40% of dietary calcium is absorbed by the average American. However, the excretion rate and absorption percentage can vary with age and physiologic state. The Recommended Dietary Allowances of calcium for Americans, then, are 360 mg for infants less than 6 months old, 540 mg for 6- to 12-month old infants, 800 mg for children aged 1 to 10 years, 1,200 mg for 11- to 18-year-old children, and 800 mg for individuals 19 years and older. During pregnancy and lactation the RDA is increased to 1,200 mg/day.

Toxicity Versus Essential Levels

Deficiency

There is no clearly defined calcium deficiency syndrome in humans. This may be due, in part, to an adaptation in calcium absorption and utilization which varies with calcium intake. In a study of 26 male prisoners ranging in age from 20 to 69 years, Malm (1958) observed that 23 of them achieved calcium balance immediately or within several months after restricting their calcium intakes from 650 or 930 mg/day to approximately 450 mg/day.

The etiology of osteoporosis, a degenerative disease involving loss of bone calcium is not clear, but prolonged inadequate intakes of calcium may play an integral role. Diets that were deficient in both calcium and vitamin D caused rickets and osteoporosis to develop in rats 6 weeks after they had been started on the diet at weaning. Osteoporosis was reversed when the rats were given a high-calcium diet that still lacked vitamin D (Gershon-Cohen and Josey, 1964). When the animals were 2 months old before receiving the low-calcium, vitamin-D-deficient diet, osteoporosis resulted without rickets.

Osteoporosis affects a large portion of older people and is most prevalent in older women. Calcium supplements that were given to osteoporosis patients for 2 years did not appear to reverse the calcium loss from bone (Shapiro *et al.*, 1975).

Hypocalcemia due to impaired alimentary adsorption of calcium in newborn children can result in tetany, consisting of twitches and spasms (Davidson et al., 1975b).

Toxicity

Calcium is relatively nontoxic when administered orally. There have been no reports of acute toxicity from the consumption of calcium that is contained in various foods. Peach (1975a) indicated that calcium intakes in excess of 1,000 mg/day when coupled with high vitamin D intakes can raise blood levels of calcium. An excess of 1,000 mg/day (2.5 times the RDA) for long periods can depress serum magnesium levels. Diets that are high in calcium have also produced symptoms of zinc deficiency in rats, chickens, and pigs after prolonged feeding. Kidney stones in humans have been associated with high calcium intakes (Hegsted, 1957).

Interactions

Low calcium intakes increase the rat's susceptibility to lead poisoning (Snowdon and Sanderson, 1974), while high intakes of calcium decrease lead absorption from the intestine (Kostial et al., 1971). Recent studies in young children have associated high blood levels of lead with low dietary intakes of calcium. Mahaffey and coworkers (1976) observed that 12- to 47-month old children with normal concentrations of lead (<0.03 mg/100 ml) in their blood had higher levels of dietary calcium (and phosphorous) than did matched children with elevated (>0.04 mg/100 ml) lead levels in their blood. Dietary calcium intake was not reported. Sorrel and coworkers (1977) found concentrations of lead and calcium in blood inversely correlated in control and lead-burdened children aged 1 to 6 years. For children with high concentrations of lead (≥0.06 mg/100 ml blood), average daily calcium intakes were 610 ± 20 mg, while children with blood lead concentrations <0.03 mg/100 ml had average daily calcium intakes of 770 ± 20 mg. Itokawa et al. (1974) suggested that the bone pain in itai itai disease in Japan was causally related to diets low in calcium and protein coupled with cadmium poisoning. Low calcium intakes increase the intestinal absorption of cadmium and the deposition of cadmium in bone and soft tissue (Pond and Walter, 1975). Furthermore, cadmium inhibits the synthesis of 1,25-dihydroxycholecalciferol by renal tubules. This hormone facilitates intestinal absorption of calcium (Suda et al., 1974), an especially important function when calcium intake is low. The same or highly similar mechanisms may control the absorption of calcium and magnesium into the bloodstream and their deposition into tissues.

Contribution of Drinking Water to Calcium Nutrition

Using an average calcium concentration in public water supplies of 26 mg/l and a maximum of 145 mg/l (Durfor and Becker, 1964) and assuming that the average adult drinks 2 l of this water daily, then the drinking water could contribute an average of 52 mg/day and a maximum of 290 mg/day. On an average basis this would represent 5% to 10% of the usual daily intake or approximately 6.5% of the adult RDA. For hard waters with high calcium levels, the water would contribute approximately 29% to 58% of the usual daily intake or approximately 36% of the adult RDA. Thus, public drinking water generally contributes a small amount to total calcium intake, but in some instances it can be a major contributor.

Conclusions

Current levels of calcium in U.S. drinking water are well below levels that pose known risks to human health. No upper limit for calcium need be set to protect public health. In cases of dietary calcium deficiencies, the presence of this element in drinking water may provide nutritional benefit.

MAGNESIUM

Presence in Food and Water

Schroeder and coworkers (1969) measured the magnesium contents of a variety of foods and foodstuffs using atomic absorption spectrophotometry. On a wet weight basis, spices, nuts, and whole grains had the highest magnesium contents and refined sugars, human milk, oils, and fats had the lowest. The food data are summarized in Table 2.

Magnesium and calcium are responsible for most of the hardness of drinking water. In a nationwide study in Canada, the mean concentration of magnesium in finished water before it entered the distribution systems was 10.99 mg/l. This concentration changed little during distribution (Neri _et_ _al_., 1977). In the United States, the mean concentration of magnesium in public water supplies in 100 cities was 6.25 mg/l (range, 0 to 120 mg/l). The concentration of magnesium in 96% of the water supplies was <20 mg/l (Durfor and Becker, 1964). From 1957 to 1969, the average magnesium concentration in U.S. surface waters was 14.3 mg/l (range, 8.5 to 137 mg/l) for 1,143 determinations (NAS, 1977).

In the United States, the average adult ingests between 240 and 480 mg of magnesium daily (Warkes _et_ _al_., 1977). Approximately 60% to 70% of this is excreted in the feces. Shils (1973) estimated the total magnesium intake of Americans and Western Europeans to be between 80 and 480

TABLE 2

Magnesium Concentrations in Foods and Foodstuffs[a]

Food Item	Magnesium Concentration, ug/g Range	 Mean
Condiments, spices	230-4,225	2,598
Nuts	1,078-3,175	1,970
Grains and cereal products	18-2,526	805
Fish and seafood	154-532	348
Meats	195-402	267
Vegetables, fresh legumes	185-297	241
fresh roots	75-478	226
fresh fleshy	66-487	174
fresh leafy	85-321	170
Dairy products, eggs	102-270	183
Fruits and juices	0.1-108	78
Sugars and syrups	2-2,526	59
Milk, human	28-29	29
Oils and fats	1-27	7
Beverages		
coffee	48	NR[b]
tea	3-11	NR[b]
whisky, gin	0.3-4.5	NR[b]
wine, white	98	NR[b]
beer	100	NR[b]
vermouth, Italian	135	NR[b]

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[a] Data from Schroeder et al., 1969.

[b] NR = Not reported.

mg/day. The British diet is reported to provide 200 to 400 mg of magnesium daily (Davidson et al., 1975a).

Requirements

The daily need for dietary magnesium is a function of the amounts of calcium, potassium, phosphate, lactose, and protein consumed. For the average healthy American on an average diet, the daily magnesium intake recommended by the Food and Nutrition Board of the National Research Council (NAS, 1974) is 60 mg for infants less than 6 months old, 70 mg for 6- to 12-month-old infants, 150 mg for 1- to 3-year-old children, 200 mg for 4- and 6-year-old children, 250 mg for 7- to 10-year-old children, and 300 mg for females 11 years and older. For adolescent and adult males the recommended dietary allowances (RDA's) are 350 mg for ages 11 to 14, 400 mg for ages 15 to 18 years, and 350 mg for those 19 years of age and older. The RDA for pregnant and lactating women is 450 mg.

Interactions

The interactions of trace elements in nutrition were reviewed in Drinking Water and Health (NAS, 1977). The metabolism of magnesium is tied closely to that of calcium and potassium. Magnesium deficiency results in potassium loss, probably due to the interaction of magnesium and phosphate in the active transport of potassium and sodium across cell membranes. The release of parathyroid hormone, calcitonin, and 1,25-dihydroxycholecalciferol, which are hormones that govern calcium and phosphorus metabolism, is reduced by lowered magnesium intakes. The mechanism for this reduction is not understood.

Toxicity versus Essential Levels

Deficiency

Despite several studies, magnesium deficiency in humans is still not well defined, primarily because it has been studied in individuals also suffering from other metabolic and physiologic disorders. Electrolyte imbalance, especially for calcium and potassium, is characteristic of magnesium deficiency.

Magnesium deficiency is most often observed in patients with gastrointestinal diseases that lead to malabsorption and in those with hyperparathyroidism, bone cancer, aldosteronism, diabetes mellitus, and thyrotoxicosis (Wacker and Parisi, 1968). Alcohol can deplete magnesium levels in heavy drinkers by apparently increasing renal loss. These heavy drinkers show extensive neuromuscular dysfunction such as tetany, generalized tonic-colonic and focal seizures, ataxia, vertigo, muscular weakness, tremors, depression, irritability, and psychotic behavior. By giving them magnesium, these dysfunctions can be reversed (Wacker and Parisi, 1968).

In the rat, prolonged magnesium deficiency retards growth and results in loss of hair, skin lesions, edema, and degeneration of the kidney (Kruse et al., 1932).

Toxicity

Because magnesium is rapidly excreted by the kidney, it is unlikely that magnesium in food and water is absorbed and accumulated in tissues in sufficient quantities to induce toxicity. Magnesium salts are used therapeutically as cathartics, e.g., magnesium sulfate ($MgSO_4$), hydroxide $[Mg(OH)_2]$, and citrate $[Mg_3][OOCCH_2COH(COO)CH_2COO]$; as antacids, e.g., magnesium hydroxide, carbonate $[Mg(CO_3)]$, and trisilicate ($Mg_2O_8Si_3$); and as anticonvulsants to control seizures associated with acute nephritis and with eclampsia of pregnancy (magnesium sulfate). In patients with renal disease and impaired magnesium excretion, large excesses of magnesium can lead to severe toxicity resulting in muscle weakness, hypotension, sedation, confusion, decreased deep tendon reflexes, respiratory paralysis, coma, and death. At plasma concentrations exceeding 9.6 mg/100 ml (8 mEq/l) central nervous system depression is evident. Anesthesia is reached near 12 mg/100 ml (10 mEq/l), and paralysis of skeletal muscle can be produced at plasma concentrations of approximately 18 mg/100 ml (15 mEq/l) (Peach, 1975a). Normal values are 1 to 3 mg/100 ml (0.8 to 2.5 mEq/l). Calcium ameliorates magnesium toxicity.

Contribution of Drinking Water to Magnesium Nutrition

Using the magnesium concentrations reported by Durfor and Becker (1964) for U.S. drinking waters (median 6.25 mg/l, maximum 120 mg/l) a daily intake of 2 l of drinking water would supply an average of approximately 12 mg of magnesium and a maximum of up to 240 mg. For Canadian (Neri et al., 1977) and Western European (Zoeteman and Brinkmann, 1977) drinking waters the daily contribution would be approximately 20 and 24 mg of magnesium, respectively. Therefore, typical drinking water in the United States, Canada or Europe provides approximately 3% to 7% of the RDA for magnesium intake by a healthy human. In areas where the magnesium concentration is high over 50% of the RDA could come from 2 l of water (see Table 32). Thus, drinking water could provide a nutritionally significant amount of magnesium for individuals consuming a diet that is marginally deficient in magnesium, especially in areas where the magnesium concentration in water is high.

Conclusions

Current levels of magnesium in U.S. drinking water supplies appear to offer no threat to human health, and no upper limit for magnesium concentrations need be set to protect public health. For individuals consuming a magnesium-deficient diet, the presence of this element in drinking water may provide nutritional benefit.

PHOSPHORUS

Presence in Food and Water

Phosphorus, in the form of phosphate, is common to most foods and foodstuffs. In foods of plant origin, phosphorus concentrates in seeds. Nuts, beans, and whole grains contain high levels of phosphorus, whereas leafy vegetables contain low levels. Fruits contain little phosphorus, but meat and fish are relatively rich in the mineral. Table 3 summarizes the phosphorus contents of some of the foods listed by Sherman (1952).

Data collected on the average daily consumption of soft drinks in the United States are summarized in Table 4. The estimates for phosphorus intakes from soft drinks indicate that such products contribute little to the phosphorus intakes for the general public. Bell and coworkers (1977) indicated that high phosphorus diets might include as much as 100 mg of phosphorus per day from soft drinks for adults.

The average daily intake of phosphorus in the United States and the United Kingdom is approximately 1,500 mg (Davidson et al., 1975b; NAS, 1974). Approximately 70% of the ingested mineral is absorbed as the free phosphate (Hegsted, 1973).

Most municipal drinking waters contain little phosphorus. Using spectrographic analysis, Durfor and Becker (1964) determined that 92% of the public water supplies of the 100 largest U.S. cities had undetectable

TABLE 3

Phosphorus Concentrations in Foods and Foodstuffs[a]

Food Item	Phosphorus Concentration, mg/100 g
Cocoa	709
Cheese, hard	610
Nuts	324-625
Beans, dry	128-586
Grains, whole	303-405
Corn	302
Fish	112-320
Meats	198-221
Eggs	210
Milk	93
Vegetables	21-92
Fruits	4-20

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[a] Data from Sherman, 1952.

TABLE 4

Estimates of Phosphorus Intakes From Soft Drink Consumption by Age Group

Age, yrs	Average Soft Drink Consumption ml/1 day [a]	Average Cola Consumption 1/day [b]	Phorphorus Intake from Cola Drinks, mg/day [c]
1-2	68	42	3
3-5	111	69	5
6-8	144	89	7
9-11	165-167	102-104	8
12-14	187-229	116-142	9-11
15-17	240-285	149-177	11-13
18-19	246-314	153-195	12-15
20-34	191-229	118-142	9-11
35-54	99-115	61-71	5
55-64	65-75	40-47	3-4
65-74	41-46	25-29	2
75+	27-38	17-24	1-2

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[a] Ranges for ages over 9 years are average values for females (lower figures) and males (higher figures). Data from USDA, 1965.

[b] Assuming that approximately 62% of all soft drinks were colas. Based on report by National Soft Drink Association (1978).

[c] Assuming the average concentration of phosphorus in colas is 0.076 mg/g drink. Based on report by Houston and Levy, 1975.

levels of phosphorus. Zoetman and Brinkmann (1977) reported that the public water supplies of 12 large cities in Europe had a mean phosphate concentration of 0.32 mg/l (0.10 mg of phosphorus) and a maximum of 3.0 mg/l (1.0 mg of phosphorus).

A survey of U.S. rivers and lakes from 1962 to 1967 indicated that 747 of the 1,577 water samples that were analyzed contained phosphorus. The mean concentration of phosphorus was 0.12 mg/l, and the maximum was 5.04 mg/l (Kopp and Kroner, 1967).

Requirements

Except for the infant, the daily allowance of phosphorus recommended by the National Research Council (NAS, 1974) is the same as that for calcium. As long as the diet contains sufficient vitamin D, the ratio of calcium to phosphorus can vary considerably. However, the ratio for the infant should be close to 1.5:1 to guard against the possible occurrence of hypocalcemic tetany during the first weeks of life (Mizrahi _et_ _al_., 1968). The recommended dietary allowance (RDA) is 240 mg of phosphorus for infants less than 6 months old and 400 mg for infants between 6 and 12 months old; for children aged 1 to 10 and adults 19 years or more, the RDA is 800 mg. Children between the ages of 11 and 18 years and pregnant and lactating women should consume 1,200 mg phosphorus daily (NAS, 1974).

Toxicity versus Essential Levels

Deficiency

Dietary deficiency of phosphorus is not known to occur in humans because of the widespread presence of the mineral in foods. Excessive use of nonabsorbable antacids can induce phosphorus depletion, which causes weakness, anorexia, and bone pain. Familial hypophosphatemia is attributed to defective absorption of the phosphate ion (PO_4) from the intestine or to defective reabsorption from the renal tubules. It is characterized by rickets and dwarfism (Glorieux _et al_., 1972; Short _et al_., 1973). There may also be decreased concentrations of erythrocyte adenosine triphosphate (ATP) and 2,3-diphosphoglycerate. In severe hypophosphatemia, acute hemolytic anemia can also occur (Jacob and Amsden, 1971; Lichtman _et al_., 1969).

Toxicity

Sodium orthophosphate (Na_3PO_4) is poorly absorbed and relatively nontoxic. Acute iatrogenic poisoning with inorganic pyro- ($Na_4P_2C_2$) or meta- ($Na_4P_4O_{12}$) phosphate salts can inhibit calcium utilization and produce nausea, diarrhea, gastrointestinal hemorrhages and ulcerations, and cellular damage in the kidney and the liver. Mazess and coworkers (1974) suggested that the high phosphate content of the diet of Eskimos may contribute to the development of osteoporosis, but this has not been confirmed. Rats fed a

5% phosphorus (as NaH_2PO_4) diet for 20 to 30 days develop renal damage. This level is 10 times the level of dietary phosphorus thought to be necessary for adequate nutrition for the rat (Duguid, 1938).

Interactions

Cations that form insoluble phosphates interfere with the absorption of phosphorus. For example, high intakes of aluminum decrease absorption of phosphorus (as phosphate) by forming insoluble aluminum phosphate ($AlPO_4$) and increasing the excretory loss of phosphorus (Ondriecka et al., 1971).

Contribution of Drinking Water to Phosphorus Nutrition

Because public drinking waters contain little phosphorus (μg/l concentrations) and because foods provide more than 1 g of phosphorus per day, it can be concluded that phosphorus levels in drinking water contribute only negligibly to human requirements for this mineral.

Conclusions

There is no nutritional basis for the regulation of phosphorus levels in U.S. drinking water supplies.

FLUORIDE

Scientific issues relating to fluoride in drinking water have been adequately defined in Drinking Water and Health (NAS, 1977). Fluoride is included in the present report only to provide complete coverage of the nutritional aspects of drinking water.

Presence in Food and Water

Fish (especially bones) and fish products are often high in fluoride. Tea is high in fluoride (a few hundred mg/kg) and two-thirds of the mineral is extracted into the infusion (Harrison, 1949). Cholak (1959) reported the fluoride concentrations in fresh foods (Table 5).

In 1962, most public water supplies of the 100 largest U.S. cities contained fluoride, according to a survey reported by Durfor and Becker (1964). Ninety-two percent of these supplies contained less than 1 mg/l (median, 0.4 mg/l; maximum, 7.0 mg/l). Of the 969 water supplies sampled in the Community Water Supply Survey of the Public Health Service (U.S. Dept. Health, Education and Welfare, 1969), the fluoride contents ranged from 0.2 to 4.40 mg/l. Fleischer and colleagues (1974) reported the fluoride contents of a variety of groundwaters: rivers contained 0.0 to 6.5 mg/l; lakes up to 1,627 mg/l; various groundwaters contained 0.0 to 35.1 mg/l; and seawater had an average concentration of 1.2 mg/l.

TABLE 5

Fluoride Concentrations in Foods and Foodstuffs [a]

Food Item	Fluoride Concentration, mg/kg
Fish	0.1 - 24
Cereals/cereal products	0.1 - 20
Meats	0.01- 7.7
Wine	0.0 - - 6.34
Vegetables	0.1 - 3.0
Eggs	0.00- 2.05
Cheese	0.13- 1.62
Coffee	0.2.- 1.6
Fruit	0.02- 1.32
Milk	0.04- 0.55
Sugar	0.10- 0.32

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[a] Data from Cholak, 1959.

Osis and coworkers (1974) determined fluoride intakes for a variety of diets in Chicago with and without fluoridation of the drinking water supply. They reported that the average daily intake of fluoride was 1.6 to 1.9 mg when the drinking water was fluoridated and approximately half this when the water was not. These values do not include the contribution made by consumption of drinking water directly but do include that added by water used for cooking. In other areas in the United States dietary intakes of fluoride ranged from 1.73 to 3.44 mg/day, and intakes of fluoride from water ranged from 0.53 to 1.27 mg/day. In four unfluoridated areas, the diet contributed 0.78 to 1.03 mg of fluoride per day and the drinking water added 0.08 to 0.44 mg/day (Kramer et al., 1974).

Wiatrowski et al. (1975) reported that the total daily fluoride intake was 0.32 mg for infants aged 1 to 4 weeks, 0.47 mg for ages 4 to 6 weeks, 0.57 mg for ages 6 to 8 weeks, 0.71 mg for ages 2 to 3 months, 1.02 mg for ages 3 to 4 months, and 1.23 mg for infants between the ages of 4 to 6 months.

Requirements

The Food and Nutrition Board of the National Research Council has not previously recommended a daily intake of fluoride (NAS, 1974), but has recently estimated adequate and safe intakes of 0.1 to 0.5 mg fluoride for infants less than 6 months of age, 0.2 to 1.0 mg for infants between 6 and 12 months, 0.5 to 1.0 mg for children between the ages of 1 and 3 years, 1.0 to 2.5 mg for 4- to 6-year-old children, 1.5 to 2.5 mg for children from 7 years to adulthood, and 1.5 to 4.0 mg for adults (NAS, in press). These levels are considered to be protective against dental caries and osteoporosis (Mertz, 1972).

Toxicity versus Essential Levels

Deficiency

Fluoride has not been shown unequivocally to be an essential element for human nutrition, except for its effectiveness in reducing the incidence of dental caries. Reports of the depression of growth in rats (Schwarz and Milne, 1972) and progressive infertility in mice (Messer et al., 1972, 1973) as consistent responses to fluoride-deficient diets have not been confirmed (Tao and Suttie, 1976; Wegner et al., 1976). The role of fluoride in dental health has been demonstrated in humans (Dean, 1941; Hodge, 1950). The incidence of dental caries was associated with low-fluoride diets, and inhibition of caries was observed in subjects who drank water containing ≥ 1.3 mg of fluoride per liter. As water intake varies with ambient temperature, so does the ingestion of fluroide. Thus, in warm climates a lower concentration of fluoride in the drinking water may be sufficient to reduce caries.

The fluoride concentration in drinking water is not critical for caries protection. Rather, it is the amount of fluoride consumed during the tooth-forming years. As the uptake and deposition of fluoride are greatest before eruption and calcification of the teeth, its anticariogenic effect is greatest with children, especially those less than 8 years old.

Toxicity

The acute and chronic toxicity of fluoride in humans was reviewed in Drinking Water and Health (NAS, 1977).

Acute poisoning by fluoride is rare in humans. Peach (1975b) estimated that a lethal dose for an adult human is approximately 5 g as sodium fluoride (NaF). The response to ingested fluoride is swift. It acts directly on the gastrointestinal mucosa causing vomiting, abdominal pain, diarrhea, convulsions, excessive salivation, and paresthesia. It also disrupts calcium-dependent functions.

Ingestion of drinking water containing excessive fluoride can result in mottling of the teeth and dental fluorosis in children. Increased density and calcification of bone (osteosclerosis) has been associated with chronic ingestion of high-fluoride water (Hodge and Smith, 1965). At unusually high levels, chronic fluoride ingestion can result in crippling skeletal fluorosis. Several studies have been conducted to determine the exact levels of fluoride at which these adverse effects occur, but the results often conflict due to lack of control or failure to account for various parameters in the study populations. Dental mottling and changes in tooth structure may develop in a few children when fluoride levels in water exceed approximately 0.7 to 1.3 mg/l, depending on ambient temperature (Richards _et al_., 1967) and diet. Roholm (1937) estimated that a 10- to 20-year daily ingestion of 20 to 80 mg fluoride could result in crippling skeletal fluorosis.

Interactions

Calcium and aluminum salts decrease the absorption of fluoride from the intestinal tract. In sheep and rats magnesium salts are somewhat less effective (Underwood, 1977; Weddle and Muhler, 1954). In studies of humans, Spencer and coworkers (1977) demonstrated that ingestion of antacids containing aluminum hydroxide [$Al(OH)_3$] increased fecal excretion of fluoride by as much as 12 times, resulting in decreased absorption and lowered plasma levels of fluoride. On the other hand, increasing calcium and phosphorus intake did not affect fluoride balance, although these latter minerals, as well as magnesium, did increase fecal excretion of fluoride.

Contribution of Drinking Water to Fluoride Nutrition

Kramer and colleagues (1974) measured the fluoride content of meals and water samples from 12 cities with fluoridated drinking water and four cities without fluoridation. From these data (Table 6), the contribution of drinking water to the individual diets can be estimated if a 2 l/day consumption is assumed. These data demonstrate that drinking water, whether artifically fluoridated or not, can make an important contribution to the total daily fluoride intake. In fluoridated areas, the contribution ranges from 25.9% to 53.5% of the total intake. In unfluoridated areas, it ranges from 13.5% to 48.1%.

Recommendations and Conclusions

Human populations should be studied in detail to determine more precisely the levels of fluoride intake (total and from drinking water) that may be causally related to dental fluorosis and osteosclerosis.

Concentrations of fluoride in drinking water that are recommended for anticariogenic effects appear to be below levels that have been associated with adverse effects in the general U.S. population. Until more precise measures of the margin of safety for the use of fluoride are available, the levels of fluoride in drinking water should not exceed the optimal levels for anticariogenic benefits.

TABLE 6

Contribution of Drinking Water to Total Daily Fluoride Intake[a]

City	Dietary mg/day	Fluoride in Water, mg/2 l daily	Contribution of Fluoride in Water to Total Fluoride Intake, %
Fluoridated Areas:			
Martinez, Calif.	1.73	1.62	48.4
Chicago, Ill.	1.97	1.90	49.1
Louisville, Ky.	1.98	2.28	53.5
St. Louis, Mo.	2.10	1.82	46.4
New York, N.Y.	2.55	1.76	40.8
Durham, N.C.	2.62	1.06	28.8
Lexington, Ky.	2.84	2.30	44.8
Madison, Wisc.	2.88	2.22	43.5
Tuscaloosa, Ala.	2.94	1.52	34.1
Cleveland, Ohio	3.05	2.54	45.4
Milwaukee, Wisc.	3.41	1.70	33.3
Corvallis, Ore.	3.44	1.20	25.9
Unfluoridated Areas:			
Birmingham, Ala.	0.78	0.16	17.0
Chicago, Ill.	0.86	0.66	43.4
Houston, Texas	0.95	0.88	48.1
Iron Mountain, Mich.	1.03	0.16	13.5

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[a] Derived from Kramer *et al.*, 1974.

SODIUM

Sodium is the most abundant cation of those found in the extracellular fluid. The sodium ion is essential to the regulation of the acid-base balance and is a very important contributor to extracellular osmolarity. It functions in the electrophysiology of cells and is required for the propagation of impulses in excitable tissues. Furthermore, sodium is essential for active nutrient transport including the active transport of glucose across the intestinal mucosa (Harper _et_ _al_., 1977).

Presence in Food and Water

The total intake of sodium is influenced mainly by the extent that salt (sodium chloride) is used as an additive to food, the inherent salt content of the foods consumed, and the intake of other sodium salts in the diet and in medications. Sodium is a natural constituent of both vegetable and animal products in varying concentrations.

In addition to salt, rich dietary sources of sodium are sodium-containing condiments such as monosodium glutamate, sauces, relishes, sweet and sour pickles, gherkins, olives, tomato ketchup, and a number of other foods including ham, bacon, sausages, dried beef, cold cuts, frankfurters, anchovies, canned crab, canned tuna, other canned fish, cheese, canned vegetables, sauerkraut, potato chips, other salted snack foods such as pretzels, rye-krisps, saltines, soda crackers, breakfast cereals, and breads such as cornbread or biscuits. The average sodium content of foods analyzed in the Food and Drug Administration's Total Diet Study (market-basket survey) for 1977 and 1978 are shown in Table 7 for typical adult intakes.

During the preservation and processing of foods, sodium and sodium chloride ($NaCl$) are added as well as any of numerous other chemical additives including sodium saccharin ($C_7H_4NO_3SNa$), monosodium glutamate [$HOOCCH(NH_2)CH_2CH_2COONa$], sodium nitrite ($NaNO_2$), sodium nitrate ($NaNO_3$), sodium benzoate ($C_6H_5COONa$), sodium ascorbate ($C_6H_7NaO_6$), sodium proprionate ($CH_3CH_2COONa$), sodium caseinate, etc. Sodium chloride or monosodium glutamate may be added to foods to suit individual tastes--not only during the commercial preparation of food but also in the home either in the kitchen or at the table. Other sources of sodium are medications, drinking water, cooking water, soft drinks, and alcoholic beverages (Newborg, 1969; Weickart, 1976). Sodium intake from carbonated beverages may be more than 200 mg/day (Table 8).

Intake of sodium chloride by American males averages an estimated 10 g/day (range, 4-24 g) (Dahl, 1960). On the basis of these estimates, which were obtained from excretion data, sodium intake would range from 1,600 to 9,600 mg/day. The average sodium intake per capita per day estimated from analysis of hospital diets has been given as 3,625 mg ± 971 (SD). This figure is for diets "as selected" and not "as

TABLE 7

Average Sodium Content by Commodity Groups in Adult Market Baskets[a]

Commodity Groups	1977 (25 Baskets)			1978 (8 Baskets)		
	mg/day	SE	% of Total	mg/day	SE	% of Total
Dairy products	704	(±15.3)	10.5	792	(±19.8)	11.4
Meat, fish, and poultry	952	(±41.2)	14.2	921	(±79.2)	13.3
Grain and cereal products	2,005	(±84.5)	29.9	2,002	(±123.1)	28.9
Potatoes	75	(± 6.2)	1.1	82	(±10.6)	1.2
Vegetables, leafy	22	(± 1.8)	--	22	(± 2.3)	--
Vegetables, legume	243	(± 8.5)	3.6	258	(±13.8)	3.7
Vegetables, roots	18	(± 1.0)	--	17	(± 3.0)	--
Vegetables, miscellaneous, and vegetable products	285	(±12.8)	4.2	284	(±42.2)	4.1
Fruits	66	(± 5.8)	1.0	75	(±14.7)	1.1
Oils, fats, and shortenings	387	(±17.1)	5.8	406	(±30.9)	5.9
Sugar and adjuncts	1,923	(±80.4)	28.7	2,042	(±123.8)	29.5
Beverages, including drinking water	17	(± 2.4)	--	27	(± 6.6)	--
TOTAL	6,697	(±130.6)		6,928	(±206.8)	

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[a] Data from Shank, 1978.

TABLE 8

Sodium Content of Soft Drinks[a,b]

Proprietary Name and Type	Sodium, mg			
	Na^+/ml	Na^+/240 ml Serving (8 oz)	Na^+/Can (360 ml;12 oz)	Calculated dail Na^+ Intake per Capita from Soft Drinks[c]
7-Up, regular	0.09	22	32	31
7-Up, sugar-free	0.14	32	48	47
Coca-Cola	0.08	20	30	29
Sprite, regular	0.18	42	62	61
Sprite, without sugar	0.18	42	62	61
PiBB, regular	0.10	23	35	34
Mr. PiBB, without sugar	0.16	37	55	54
Fanta, orange	0.09	21	31	30
Fanta, grape	0.09	21	31	30
Fanta, root beer	0.10	23	35	34
Fanta, ginger ale	0.13	30	46	45
Fresca	0.24	57	85	83
Tab	0.13	30	46	45
Tab, black cherry	0.20	48	72	71
Tab, root beer	0.18	42	62	61
Tab, ginger ale	0.20	47	71	70
Tab, orange	0.18	43	65	64
Tab, grape	0.19	44	65	65
Tab, lemon-lime	0.18	42	62	61
Tab, strawberry	0.17	39	59	58

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[a] Values for sodium content of soft drinks varies with sodium content of the water that is used during manufacture.

[b] Information derived from the Consumer Information Center, Coca Cola Company, Atlanta, Georgia, and the Seven-Up Company.

[c] Based on 1977 estimate of per capita annual consumption of soft drinks at 359 12-oz units (98% of a 12oz can/day). Personal communication from the National Soft Drink Association, Washington, D.C. Sales Survey of the Soft Drink Industry.

eaten" and does not include salt that may have been added at the table (California State Dept. of Public Health, 1970). Sodium intake by infants depends on milk source, formula composition, and the amount of salt added as seasoning by the preparer.

The sodium content of drinking water is extremely variable. Greathouse and Craun (1979) reported that levels of sodium in household tap waters were above detection limits in 99.79% of the areas sampled. The maximum sodium concentration was approximately 80 mg/l, the minimum was approximately 4.0 mg/l, and the mean concentration was approximately 28 mg/l (Craun et al., 1977).

Raw water samples were analyzed by the U.S. Environmental Protection Agency Region V Laboratory and Indiana State University (USEPA, 1975) during 1971-1975. The sodium content was between 1.1 and 77.0 mg/l. Finished drinking water samples, which were also analyzed by these same groups, had sodium contents of 1.0 to 91.0 mg/l.

In a survey of community water systems undertaken as a cooperative study by the New York State Department of Health (1977) and the U.S. Department of Interior, Geological Survey, approximately 12% of the water samples analyzed contained sodium concentrations in excess of 20 mg/l. The highest concentraton of sodium in drinking water recorded in this survey was 220 mg/l in two systems, one in Chemung County and one in Wayne County. The report of this study pointed out that sodium is added during the treatment of public water supplies as follows:

1. Ion exchange softening--sodium ion in an exchange medium. Sodium, in the forms of sodium chloride, sodium carbonate (Na_2CO_3), and sodium hexametaphosphate [$(NaPC_3)_x$], is exchanged for magnesium and calcium.

2. Chemical precipitation softening--sodium carbonate (soda ash)

3. Disinfection (chlorination)--sodium hypochlorite ($NaOCl$).

4. Fluoridation--sodium fluoride (NaF) or sodium silicofluoride (Na_2SiF_6).

5. Corrosion control--sodium carbonate or sodium hexametaphosphate.

6. pH adjustment--sodium carbonate or sodium hydroxide ($NaOH$).

7. Coagulation--sodium aluminate ($NaAlO_2$) or sodium silicate ($NaSiO_3$).

8. Dechlorination--sodium bisulfite ($NaHSO_3$).

Many residences with public water or individual well-water supplies also have water-softening units that can add sodium to the water. In most home water-softening units, the ion-exchange process is used. This process increases the sodium concentration in the finished water since it adds two atoms of sodium for every atom of calcium removed.

To summarize the distribution of sodium in New York State water supplies, 265 community water systems had a sodium content between 5.01 and 20.00 mg/l, 57 such systems contained between 20.01 and 50.00 mg/l, and 32 systems, which served a total of 22,080 people, contained more than 50.01 mg/l (New York State Department of Health, 1977).

Requirements

The estimated adequate and safe intakes for sodium range from 1,100 to 3,300 mg/day for normal adults or 1 g of sodium per kilogram of fluid and food intake (Meneely and Battarbee, 1976; NAS, in press). In infants, estimated adequate and safe intakes are approximately 115 to 750 mg/day (NAS, in press).

Toxicity versus Essential Levels

Acute Toxicity

Salt poisoning or acute sodium toxicity is produced by massive overload, particularly in the very young. In Broome County, New York, six out of 14 infants exposed to a sodium concentration of 21,140 mg/l died when salt was mistakenly used in place of sugar in their formulas (Finberg et al., 1963). Acute toxicity with sodium chloride in healthy adult males accompanied by visible edema may occur with an intake of 35-40 g of salt per day (Meneely and Battarbee, 1976).

Chronic Toxicity

Evidence suggests that chronic excessive intake of sodium may be associated with hypertension, which is defined on the basis of blood pressure readings, i.e., mild hypertension implies diastolic blood pressure above 90 mm Hg and systolic blood pressure above 140 mm Hg (Reader, 1978). In populations residing in different geographic areas, a positive correlation has been found between salt intake and the incidence of hypertension (Dahl, 1972; Sasaki, 1962).

Sodium toxicity leading to hypertension has been associated with intakes of salt (NaCl) greater than 30 g/day, but may occur at lower intakes in persons predisposed to hypertension or suffering from hypertension, congestive heart failure, cirrhosis, or renal disease. Toxicity of sodium salts may be influenced by the anion with which sodium is paired (Venugopal and Luckey, 1978). Until recently, the failure to demonstrate a causal relationship between salt intake and the development of hypertension has discouraged scientists from recommending limitation of salt intake according to the Advisory Panel of the British Committee on Medical Aspects of Food Policy (Nutrition) on Diet in Relation to Cardiovascular and Cerebral Vascular Disease (1975).

The level of sodium in drinking water may influence blood pressure. The blood pressure distribution patterns for systolic and diastolic pressures of high school students living in a community with elevated levels of sodium in the drinking water (100 mg/l) showed a significant upward shift as compared with the patterns for matched students in a neighboring community with low sodium levels in the drinking water (8 mg/l) (Calabrase and Tuthill, 1977).

Twenty percent of the adult U.S. population has hypertension (Intersociety Commission for Heart Disease Resources, 1971). In the treatment of essential hypertension, restriction of dietary sodium leads to a fall in blood pressure (Allen and Sherrill, 1922). Dahl et al. (1958) reported that weight reduction in obese individuals leads to a decrease in blood pressure only when sodium intake is restricted. On the other hand, sodium restriction in the obese significantly reduces blood pressure even when calories are not restricted.

In hypertensive subjects, a lowering of blood pressure may be effected either by reducing total sodium intake or by using of thiazide diuretics, which promote sodium excretion. In 1960, the American Heart Association (AHA) reported that diuretics could reduce the need for a very restricted sodium diet and that they produced quick results, a desirable factor when there is an acute need for lowering blood pressure. The AHA advocated a sodium-restricted diet for the long-term management of hypertension (Pollack, 1960).

A maximum level of sodium in drinking water of 20 mg/l has been suggested by the American Heart Association (1957).

Currently antihypertensive medication, including diuretics, is considered a requirement in the management of established hypertension. Sodium restriction alone can control borderline hypertension thereby reducing the need for diuretics (AMA, 1973; Mayeer, 1971).

According to Freis (1976), the consumption of less than 5 g of salt a day might reduce the incidence of hypertension and its related diseases by 80% but the evidence available to support such specific figures is limited. Blackburn (1978) suggested a public health intervention trial "to test...reduced sodium consumption and culture-wide changes in salt-eating habits as a long-term public health approach to primary prevention of hypertension."

Sodium-restricted diets are required in the treatment of congestive cardiac failure, renal disease, cirrhosis of the liver, toxemia of pregnancy, and Meniere's disease. Sodium-restricted diets may also be required for patients on prolonged corticosteroid therapy. Moderate sodium restriction has been advocated for the management of pre-menstrual retention associated with fluid retention (Wintrobe et al., 1970).

Clinical experience has shown that patients often do not adhere to prescribed sodium-restricted diets. However, it is difficult to check compliance from dietary records since patients either forget that certain foods contain appreciable amounts of sodium or are unaware of sodium sources in foods, in drugs, or in water. Pietinen et al. (1976) proposed the use of mean urinary sodium values (mean of three 9-hour overnight urinary sodium estimations) to check compliance with dietary suggestions.

In Australia, Morgan et al. (1978) treated patients with mild hypertension by moderately restricting their salt intake, which was monitored by checking urinary sodium values. Results were compared with those of a control group and a group maintained on antihypertensive medication. Salt restriction reduced the diastolic blood pressure by 7.3 ± 1.6 mm Hg, a result similar to that of patients treated with the antihypertensive drugs. In the untreated group, the diastolic blood pressure rose by 1.8 ± 1.1 mm Hg. The authors pointed out that most patients did not achieve the amount of salt restriction their physicians desired and inferred that stricter adherence to the diet could have caused further reductions in blood pressure. To effect restriction of sodium intake, they recommended the avoidance of both salted foods and addition of salt to food at the table. However, they acknowledged that it would be difficult be difficult to reduce the intake of sodium below approximately 2,300 mg/day in Australia because of the widespread use of sodium salts in prepared foods (Morgan et al., 1978). This is also probably true in the United States. (See Table 7.)

Elliott and Alexander (1961) reported adverse health effects in persons on sodium-restricted diets when they consumed water with a high sodium content. The authors observed recurrent episodes of heart failure which ceased when water with a low sodium content was substituted.

Deficiency

Sodium deficiency may result from renal disease, diuretic therapy, osmotic diuresis, adrenal insufficiency, vomiting, diarrhea, wound drainage, excessive sweating, burns, mucoviscidosis (cystic fibrosis), peritoneal drainage, and pleural, pancreatic, and biliary fistulae drainage. Salt restriction leads to sodium deficiency under conditions of renal impairment.

Sodium depletion can be either iatrogenic or noniatrogenic. Iatrogenic causes include administration of excessive amounts of free water, thiazides, other diuretics, such as furosemide and ethacrynic acid, barbiturates, and oral hypoglycemic drugs (de Bodo and Prescott, 1945; Fishman et al., 1971; Fuisz, 1963; Stormont and Waterhouse, 1961).

Noniatrogenic causes of hyponatremia are commonly related to the inability to excrete free water which is either administered or generated from endogenous sources. Hyponatremia can also be induced by poor secretion of antidiuretic hormones, alcoholic cirrhosis, adrenocortical insufficiency, congestive heart failure, and cachexia (Bartter and Schwartz, 1967; Birkenfeld et al., 1958; Kleeman, 1971; Matter et al., 1964).

Drinkers of large quantities of beer who eat very little food can experience fatigue, dizziness, and muscle weakness.

These patients are both hyponatremic and hypokalemic. The syndrome is rapidly resolved by abstaining from beer consumption and eating a normal diet. Hilden and Svendsen (1975) stated that beer is often low in sodium (20-50 mg/1), that the patients did not obtain adequate sodium or potassium from their diets, and that water diuresis is inhibited and hyponatremia develops when animals or humans are kept on a sodium-deficient regimen.

Arieff et al. (1976) discussed the neurological symptoms of hyponatremia. In addition to nonneurological symptoms (anorexia, nausea, vomiting, and muscle weakness), 14 patients with acute hyponatremia had some depression of the sensorium and four of them had grand mal seizures. Seven of these patients were treated with hypertonic saline while four were treated only with fluid restriction. Of the seven patients that were treated with hypertonic saline, five survived. Three of the four patients treated with fluid restriction died. The authors emphasized that edema of the brain that may occur with hyponatremia may go undiagnosed.

Sweat is a major route for sodium losses. Consolazio et al. (1963) studied three normal young men who were made to sweat by daily exercise on a stationary bicycle at temperature of 24°C or 37.8°C. Sweat was collected in arm bags made of polyethylene. The percentage of total sodium excretion that was excreted in sweat was 62.8% in 7.5 hours and 88.7% in 16.5 hours. The sodium content of sweat varies from approximately 500-1,200 mg/l. Lower values result if subjects have been acclimatized to heat. Lee (1964) reported that excessive sweating, which can be brought on by exercise, heat, or fever, can result in sodium losses from the skin as high as 7 g/day. He suggested that sodium chloride be administred to prevent hyponatremia whenever more than a 4-liter intake of water is required to replace sweat losses. Furthermore, he recommended that 2 g of sodium chloride be given for each additional liter of water lost. This would amount to approximately 7 g/day for people doing heavy work in extreme heat (Lee, 1964). People who are exposed to high temperatures occupationally or during leisure and those performing heavy physical work may find it convenient to take salt pills or to add sodium chloride to their drinking water.

Interactions

Potassium chloride (KCl) counteracts the hypertensive effects of chronic excess of sodium chloride. Lithium from lithium carbonate (Li_2CO_3) accumulates in the body of sodium-depleted persons (Meneely and Battarbee, 1976).

Contributions of Water to Sodium Nutrition

Given an intake of 2 liters of drinking water per day with a mean sodium concentration of 28 mg/l, a contribution of sodium in water to the estimated adequate and safe intake would be approximately 1.7-5.0%. The contribution of sodium at 28 mg/l in water to the observed current dietary sodium intake is between 0.6% and 3.4%. (These figures do not take into account sodium sources from medication, and they refer to adults only.)

Conclusions

Table 10 (placed after the section on Iodine) summarizes information on sodium in water and the diet.

Data suggest that whereas health benefits could accrue to certain segments of the population from reduction in sodium intakes, the amount of sodium contributed to the intake from drinking water is small except for persons on sodium-restricted diets (<2,000 mg/day). According to the National Center for Health Statistics, approximately 2.8% of Americans are on low sodium diets (NAS, 1977). The size of the population that is predisposed towards hypertension when exposed to elevated sodium intake is not known with any certainty.

Options available to reduce sodium intake are (in order of decreasing potential) reducing salt added to food as seasoning when eating or cooking, consuming foods with lower sodium levels, reducing sodium in drugs and additives, or reducing sodium levels in water.

Recommendations

Research is needed to define more exactly the contributions of sodium intake, sodium-potassium intake ratios, and other physiological factors to the development of hypertension.

The relationship of the level of sodium and the sodium/potassium ratio in drinking water to blood pressure should be investigated further.

The level of sodium in drinking water should be monitored and physicians informed of the level via local public health departments.

The sodium content of drinking water should not be increased purposefully. Safeguards should be taken against accidental increases, e.g., salting of roads in winter resulting in "deicing" runoff. In instances where water is to be softened (by ion-exchange) domestically, a three-line system is recommended so that only the water used for bathing and laundry would be softened--not the water for drinking.

Total review of the sources of sodium intake is urgently required along with publication of the sodium content of drinking water, beverages, foods, and drugs.

POTASSIUM

Potassium has four major biological functions. It contributes to the maintenance of electrolyte balance, the transmission of nerve impulses to muscle fibers and the control of normal muscle contractility, and the control of heart rhythm, and it acts as an insulin antagonist in intermediary carbohydrate metabolism.

Presence in Food and Water

According to Greathouse and Craun (1979), the mean concentration of potassium in household tap waters is 2.15 mg/l (min, 0.721 mg/l; max, 8.278 mg/l). Concentrations of potassium in drinking water in Region V (defined by the U.S. Environmental Protection Agency) were 0.5 to 7.4 mg/l in raw water and 0.5 to 7.7 mg/l in finished water (USEPA, 1975).

Potassium is widely distributed in foods, both as a natural constituent and as an ingredient in food additives. In foods of plant origin, the commonest naturally occurring anions of potassium salts are nitrate (KNO_3), sulfate (K_2SO_4), phosphates (K_2HPO_4, KH_2PO_4, or K_3PO_4), and chloride (KCl). Amounts of these potassium salts vary with the plant as well as with methods of cultivation and fertilization (Grunes, 1978, personal communication).

Potassium-containing food additives include potassium alginate (a stabilizer, thickener, and emulsifier), potassium chloride [a gelling agent and a substitute for sodium chloride ($NaCl$)], potassium iodate (KIO_3) and potassium bromate ($KBrO_3$) (dough conditioners that are added to bread mixes), potassium nitrate used as a food preservative, monobasic and dibasic potassium phosphates (buffering agents and sequestrants), tribasic potassium phosphate (an emulsifier), potassium polymetaphosphate [$(KPO_3)_x$] (a fat emulsifier and moisture retaining agent), potassium pyrophosphate ($K_4P_2O_7$) (an emulsifier and texturizer), potassium sorbate ($CH_3CH{=}CHCH{=}CHCOOK$) (a preservative), potassium sulfate (a water corrective agent), and potassium bitartrate or cream of tartar ($KHC_4H_4O_6$) (an acidifying agent) (NAS, 1972).

Rich food sources of potassium are bran, dried brewer's yeast, cocoa, instant coffee, dried legumes, teas, spices, molasses, almonds, peanuts, raisins, peanut butter, avocado, pear, stewed prunes, parsley, bananas, potatoes, butter beans, dried, whole or nonfat milk, chocolate milk, oranges, orange juice, squash, and melon. Potassium is highly available in food.

The Food and Drug Administration's Total Diet Study ("Market Basket" Survey) estimates of potassium intakes in the United States for three age groups for 1977 and 1978 are shown in Table 9.

Current dietary potassium intakes of adults are believed to range from 1,500 to 6,000 mg/day.

Dietary items with a very high potassium content may be consumed infrequently by young children and the elderly

TABLE 9

FDA Total Diet Study ("Market-Basket") Estimates of Potassium Intake[a]

Age	Classification	Intake, mg/day 1977	1978
6 months	Infants	1,551	1,590
2 years	Toddlers	1,714	1,846
15-29 years	Adults	4,549	4,735

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[a] Data from Shank, 1978. Values are based on an intake of 3900 Calories/day.

(Wilson et al., 1966). Younger men and women obtain enough potassium from their diets to satisfy nutriticral requirements (Wilde, 1962).

Requirements

The estimated adequate and safe intake of potassium for adults is between 1,875 and 5,600 mg/day. Intkaes for infants and children are given in Table 31 at the end of this report (NAS, in press).

Toxicity versus Essential Levels

Deficiency

Older persons may have low potassium intakes. In a study of 46 men and 88 women aged 65 and over, who lived in their own homes in northern Glasgow, Judge et al. (1974) observed that the mean dietary potassium intake for men was 2,769 mg/day and for women, 2,106 mg/day.

A gross reduction in dietary potassium intake can produce potassium depletion and a drop in serum potassium levels (Squires and Huth, 1959; Womersley and Darragh, 1955). Mohamed (1976) also observed low potassium intakes among elderly pensioners in southern Sweden. He analyzed actual food portions and beverages.

In an unpublished study of the diets of elderly housebound women and men in New York State during 1978, Roe (personal communication) discovered that the mean potassium intake was 2,071 mg/day (median, 1,893 mg/day; minimum, 703 mg/day; and maximum, 4,178 mg/day. Judge and Cowen (1971) showed that elderly people whose dietary intakes of potassium are less than 2,340 mg/day may have reduced handgrip strength. Overt potassium deficiency in adults is associated with intakes of 2,000 mg or less per day.

Major causes of potassium deficiency include prolonged vomiting or diarrhea, starvation, diabetic acidosis, surgery, use of diuretic drugs, use and abuse of cathartics, and intakes of corticosteroid hormones (FDA, 1975; Krause and Hunscher, 1972; Robinson, 1967).

Nardone et al. (1978) estimated that approximately 98% of total body potassium is contained in the intracellular compartment of the body. Less than 2% is located in the serum where it can be extracted for measurement. Low serum potassium levels usually reflect total body deficit. However, in alkalosis, insulin therapy and hypoosmolality may decrease serum levels of potassium (without a concomitant decrease in cellular potassium) so that they do not reflect actual body stores (Nardone et al., 1978).

Potassium is excreted through the urine, gut, and skin. According to Nardone et al. (1978), the losses through the gastrointestinal tract and the skin are relatively minor under physiologic conditions (Berliner, 1960; Suki, 1976).

Nardone et al. (1978) classified the origins of hypokalemia as follows:

- Gastrointestinal malabsorption

- Renal loss of potassium due to disease
- Loss of potassium induced by drugs (e.g., diuretics, including organomercurials, thiazides, furosemide, and ethacrynic acid; antibiotics, including carbenicillin and penicillin; laxatives; corticosteroids; and nephrotoxic drugs, e.g., outdated tetracycline) and by licorice and extracts of licorice
- Maldistribution of potassium caused by periodic paralysis (familial, acquired), drugs (e.g., insulin), and toxins (e.g., barium)

Drug-induced hypokalemia is extremely common. Hypokalemia resulting from low intake is less common. Several disorders, e.g., cancer, gross neurological disease, psychiatric illness, and chronic gastrointestinal disease, reduce total food intake and, thus, potassium intake. They can also lead to hypokalemia because of catabolism.

Hypokalemia can result from self-administration of excessive quantitites of diuretics, laxatives, or licorice, or from self-induced vomiting. Patients who induce hypokalemia by these means usually have an underlying psychiatric illness. In the young, this illness may be anorexia nervosa (Fleming *et al*., 1975; Katz *et al*., 1972; Wallace *et al*., 1968; Wrong and Richards, 1968).

Symptoms of potassium deficiency are weakness, anorexia, nausea, vomiting, listlessness, apprehension, and sometimes diffused pain, drowsiness, stupor, and irrationality. Hypokalemia can exist without any abnormal clinical findings. When symptoms are present, the most common is profound muscle weakness. Changes in electrocardiograms are also found (Zintel, 1968).

In hypertensive patients who are maintained on diuretics, potassium chloride can be used as a salt substitute to reduce sodium intake while providing a source of potassium.

Potassium depletion sensitizes patients to intoxication by cardiac glycosides such as digitalis. Potassium deficiency causes both structural damage and functional impairment of the kidney.

Toxicity

Keith et al. (1942) investigated effects of single large doses of potassium salts in seven normal persons. These subjects ingested from 12.5 to 17.5 g of potassium chloride or bicarbonate ($KHCO_3$). Their renal clearances were then determined. In two subjects, the potassium load disturbed normal renal excretion. The authors estimated that single doses of potassium salts containing 80-100 mg of potassium per kilogram of body weight may be nephrotoxic. Extracellular potassium, if rapidly raised by intravenous injection from 125 to 2,500 mg/l, is toxic and may be lethal (Comar and Bronner, 1962).

It is not possible to produce hyperkalemia or potassium toxicity by dietary means in people with normal circulatory and renal function (Burton, 1965). Hyperkalemia is caused mainly by diseases such as Addison's disease or by renal failure with gross oliguria. Potassium toxicity can be caused by ingestion of enteric-coated potassium chloride tablets. Symptoms of this toxicity include gastric irritation, ulceration of the small intestine, and perforation of late strictures (Mudge and Welt, 1975).

Malabsorption of vitamin B_{12} has been identified in patients receiving slow-release potassium chloride supplements. Schilling test values of vitamin B_{12} absorption were normalized when potassium chloride was withdrawn from the regimens of these patients (Palva et al., 1972).

Symptoms of acute poisoning caused by eight 4-g potassium chloride tables were cyanosis, shallow respiration (Keith et al., 1942), and life-threatening cardiac arrhythmia (Maxwell and Kleeman, 1972). According to Blum (1920), 25 g of potassium chloride per day can induce acute toxicity. Smaller doses can cause diarrhea. Intakes of potassium associated with acute toxicity are 7-10 g/day in adults and 2 g/day in young children.

Interactions

Metabolism of protein, amino acids, and glucose are affected by potassium status (Lehninger, 1971).

Focusing attention on the high sodium, low potassium environment in our society, Meneely and Battarbee (1976) and Meneely and Ball (1958) presented evidence that reduced sodium intake with a concurrent increase in potassium intake would benefit health, particularly for hypertensive or borderline hypertensive subjects. Potassium has a protective action against the hypertensive effect of high sodium intakes in humans and in laboratory animals, but the mechanism is unknown (NAS, 1970).

Contributions of Drinking Water to Potassium Nutrition

Because the levels of potassium in water are low in relation to those in foods, the contribution of water to the requirement or intake of potassium is negligible.

Conclusions

Table 10 (in the section on Iodine) summarizes information on potassium in drinking water and the diet.

Potassium is abundant in the food supply, whereas water contributes little to total potassium intake.

Potassium deficiency is common in certain subgroups of the population, notably the elderly whose potassium deficiency is attributed to low intake of potassium-rich foods as well as to the use of laxatives and diuretics. Potassium deficiency is a cause of geriatric disability including severe muscle weakness. Frequently it also produces digitalis toxicity, which is life-threatening.

Potassium excess leading to toxicity is not common and is not incurred through the diet. Acute potassium toxicity can be induced by oral potassium preparations including enteric-coated pills.

Research Recommendation

Studies should be directed towards defining more closely the RDA for potassium in different age groups particularly the elderly.

CHLORIDE

Chloride is the most important anion in the maintenance of fluid and electrolyte balance and is necessary to the formation of the hydrochloric acid (HCl) in the gastric juices.

Presence in Food and Water

Rich sources of chloride are salt, breakfast cereals, breads, dried skim milk, teas, eggs, margarine, salted butter, bacon, ham, salted beef (corned beef), canned meats, canned fish, canned vegetables, salted snack foods, and olives. In the diet, chloride occurs mainly as sodium chloride (NaCl) (Harper _et_ _al_., 1977)).

Chloride is found in practically all natural waters. Surface waters contain only a few milligams per liter, whereas streams in arid or semiarid regions contain several hundred milligrams per liter, especially in drained areas where chlorides occur in natural deposits or are concentrated in soils through evaporation processes. Contamination with sewage increases the chloride content of river waters. Industrial wastes and drainage from oil wells or other deep wells and from salt springs may add large quantitites of chloride to streams. Most public water supplies contain less than 25 mg/l. Groundwater usually contains larger quantities than surface waters. Some public supply wells may contain as much as 100 mg/l.

In the 1975 report on the Region V survey of the contents of selected drinking water supplies (USEPA, 1975), the mean concentration of chloride in raw water was 18 mg/l (SD ± 17) and the content of finished water was 21 mg/l (SD ±21). Concentations as high as 179 mg/l were recorded although 95% of the samples analyzed fell below 40 mg/l. In a chemical analysis of Interstate Carrier Water Supply Systems (USEPA, 1975), 11 of 684 samples (1.6%) failed to meet the recommended drinking water limit for chloride which was set in 1962 by the U.S. Public Health Service at 250 mg/l (USPHS, 1962).

The U.S. Environmental Protection Agency has similarly set the secondary maximum contaminant level for chloride content in drinking water at 250 mg/l (USEPA, 1977) based on findings that are described below.

The presence of particular concentrations of chloride ion (Cl^-) in drinking water can produce a taste that is sometimes objectionable to the consumer. Water may be rejected on the basis of its chloride content. Whipple (1907) reported that subjects showed a differential ability to detect the chloride content of water which varied with type of chloride salt added. The chloride content of the water sampled by his subjects ranged from 96 to 560 mg/l.

Lockhart et al. (1955) reported that taste thresholds for the chloride anion in water varied from 210 to 310 mg/l, according to the type of chloride salt added. They noted that a high chloride content of water may cause an unpleasant taste in coffee. Richter and Maclean (1939) found that the chloride taste threshold was lower than that found by other authors.

Current dietary intakes vary largely with intake of salt. Estimates range from 2,400 to 14,400 mg/day for sodium chloride (Dahl, 1960).

Distribution in Tissues

According to Forbes (1962), the chloride concentration in humans is approximately 2,00 mg/kg of fat-free body mass in the newborn and 1,920 mg/kg in the adult. Ziegler and Fomon (1974) believe it is reasonable to assume that the concentration of chloride in fat-free body weight gain after birth is approximately 1,920 mg/kg.

Requirements

The essentiality of chloride is generally recognized but no recommended dietary allowances (RDA's) for it have been determined.

Ziegler and Fomon (1974) suggested that the chloride requirements for growth (alone) was 28 mg/day from birth to 4 months of age, 21 mg/day from 4 months to 12 months, 12 mg/day from 12 months to 24 months, and 12 mg/day from 24 months to 36 months. Advisable total intakes of chloride for infants in these four age groups are 245 mg/day, 210 mg/day, 245 mg/day, and 350 mg/day, respectively. A daily chloride turnover in adults (intake/output) ranges from between 85 and 250 mEq. Cotlove and Hogben (1962) found that the loss of chloride generally parallels that of sodium.

Toxicity versus Essential Levels

Imbalance and Depletion

Electrolyte imbalances may disturb the absolute or relative amounts of chloride in the serum. Abnormalities of sodium metabolism are usually accompanied by abnormalities of chloride metabolism. When there are high losses of sodium, as in diarrhea, profuse sweating, or certain endocrine abnormalities, chloride deficit is also observed. However, when there is loss of gastric juice through vomiting, losses of chloride exceed sodium losses. This leads to a decrease in plasma chloride and a compensatory increase in bicarbonate (HCO_3^-). This results in hypochloremic alkalosis (Lennon, 1972). In Cushing's disease, or after the administration of an excess of corticotropin (ACTH), cortisone, or other corticosteroids, hypokalemia with an accompanying hypochloremic alkalosis may occur. Hypochloremia may also result when chloride is lost through profuse diarrhea, which impairs the reabsorption of chloride in the intestinal secretion (Harper *et al.*, 1977).

Toxicity

The toxicity of salt containing the chloride ion depends mainly on the characteristics of the cation. Administration of hydrochloric acid (HCl), ammonium chloride (NH_4Cl), lysine hydrochloride $[NH_3(CH_2)_4CH(NH_2)COOH]^+[Cl]^-$, or arginine hydrochloride $[HN{=}C(NH_3)NH(CH_2)_3CH(NH_2)COOH]^+[Cl]^-$ adds to the quantity of readily dissociated acid (HCl) but is buffered by the bicarbonate ion (HCO_3) leading to an increase in the plasma concentration of chloride and a decrease in plasma bicarbonate. This results in hyperkalemic metabolic acidosis.

Effects of Chloride Loading

Adaptation to sodium chloride load may occur in human subjects. In experiments on isolated frog skin, Watlington *et al*. (1977) showed that extracts of the urine of humans on a high sodium chloride intake produced a net active-transport of mediated chloride ion efflux. On the other hand, such activity was not induced by the urine of either normal humans who had been deprived of sodium and humans with adrenal insufficiency who had been loaded. These findings suggest the presence of an adrenal corticosteroid, which may participate in adaptation to high salt intake.

Interactions

Normally, the only halogen in the extracellular fluid is chloride. Chloride may be partially replaced by bromide when bromide is taken as a medication over a prolonged period. Each mEq of bromide retained displaces 1 mEq of chloride, but total halide, i.e., total chloride and bromide concentration, remains unchanged. Many of the chemical and biological properties of chloride and bromide are similar, but renal tubular transport differs. The renal clearance of bromide is slightly less than that of chloride indicating that the tubular epithelim retains bromide preferentially. A progressive rise in bromide and falling chloride concentrations result from long-term ingestion of rather small doses of bromide. Chronic bromism is treated by increasing urinary bromide excretion. Any treatment that increases chloride losses will also result in increased bromide losses. Therefore, administration of a chloride source, e.g., sodium chloride, and such diuretics as furosemide ($C_{12}H_{11}ClN_2C_5S$) and ethacrynic acid ($C_{13}H_{12}Cl_2C_4$) have been used to treat bromism (Emmett and Narins, 1977).

The Contribution of Water to Chloride Nutrition

Since no recommended dietary allowance (RDA) exists for chloride it is not possible to assess the contributions of drinking water to the nutritional requirement for chloride.

A typical chloride concentration in drinking water of 21 mg/l would contribute 42 mg/day (assuming a 2 l/day consumption). This would be just under 2% of the lower estimates of total chloride intake. The highest chloride concentration observed (179 mg/l) would contribute 15% to the lowest total intake.

Conclusions

The chloride content of waters varies with the geochemistry of the area and contamination from sewage, industrial, or other wastes.

Concentrations above 250 mg/l chloride cause a salty taste in water which is objectionable to many people.

Consumption of chloride in reasonable concentrations is not harmful to most people. However, if the chloride is present as sodium chloride, the sodium ion may be undesirable to persons requiring salt restriction.

Typical chloride concentrations in drinking water contribute relatively little to total chloride intakes.

Research Recommendations

Representative chloride intakes from water and food should be determined by region, by locality, and by sex/age groups.

Implications of high chloride ingestion require further investigation.

Means of minimizing the entry of excess chloride into drinking water supplies should be studied.

IODINE

In this section the term iodine, when used in a general sense, denotes all iodine-containing compounds, e.g., iodate (IO_3^-), iodide (I^-), etc.

Iodine is an essential micronutrient. It is an integral constituent of the thyroid hormones, thyroxine and triiodothyronine, which have important endocrine functions in metabolic regulation.

Presence in Food and Water

Sources of iodine include foods, water, internal and topical medications, and air (Underwood, 1971). In the United States, the major contributions to iodine intake come from iodized salt, bread, milk, marine fish, and seafood. Eggs, other animal protein foods, the food coloring erythrosine, water, human milk, kelp, vitamin-mineral supplements, and formula foods also contain iodine. These dietary sources of iodine are highly available as indicated by relationships between intake and urinary excretion of iodine (Kidd et al., 1974).

The origins of iodine in foods are soils, water, commercial fertilizers, atmospheric iodine, iodine-containing antiseptics, food additives, and food or water pollutants. Major sources of iodine in milk are the iodophors--iodine-containing antiseptics that are used to cleanse the cows' udders and to "sterilize" milking equipment or food preparation areas. The Wisconsin Alumni Research Foundation (WARF Institute, 1977) reported high iodine concentrations in milk shakes that were prepared in fast-food restaurants.

Iodine in seafoods is derived from ocean waters, which contain approximately 0.06 mg/l, mainly as iodate, but also as iodide. Breads contain a variable amount of iodine, depending on the source and means of production. Breads made with dough conditioners consisting of calcium or potassium iodate [$Ca(IO_3)_2$, KIO_3] contain much higher iodine concentrations. Breads made by a continuous mixing process with iodate have a higher iodine content than those produced by conventional mixing with iodate (Hemken et al., 1972; Kidd et al., 1974; NAS, 1974a).

Erythrosine (the disodium salt of tetraiodofluorescein), a food-coloring agent, contributes iodine to the diet when it is used in the manufacture of certain breakfast cereals and other foods such as fruit jellies (Vought et al., 1972).

Table salt is iodized to furnish 76 μg of iodine per gram of salt. As of 1968, 54.8% of the table salt sold in the United States was iodized. Use of iodized salt varies with region of the country. The amount of iodide added to the diet via table salt is extremely variable, not only because of differences in the use of iodized vs. noniodized salt, but also because salt intake varies markedly. In a population containing both high and low salt users, it is difficult to use the average intake of salt at 10 g/day/person (NAS, 1974b) to calculate intakes of iodine from salt.

Iodine in marine fish and shellfish is presumably derived from sea water and, especially, from marine plants, which have the highest concentrations of iodine of any plant species (Chilean Iodine Education Bureau, 1950).

Drinking water contains a small and variable amount of iodine, which is determined by location, water treatment processes used, and the degree of pollution. Among water-processing methods, flocculation with alum and sedimentation appear to reduce iodine content. Chlorination, when used alone, results in only a small loss of iodine (<10% reduction in the iodine content of raw water).

Iodine enters drinking water from atmospheric iodine (via rain or snow), soil, and, in the case of polluted drinking waters, from decaying plants, animal excretions, and commercial fertilizers. Water containing feces, urine, or plant debris contains more iodine than unpolluted water from the same area (Vought _et_ _al_., 1970).

Freshwater contains 0-2.4 μg/l in areas where goiter is endemic and 8-9 μg/l in goiter-free areas (Fisher and Carr, 1974). Surface water, more often consumed by domestic animals, contains 4-336 μg/l (NAS, 1974b).

Concentrations of iodine at 4 to 8 μg/l in raw (untreated) water and 3.4 to 3.8 μg/l in treated water, both in Potomac, Md., and up to 18 μg/l in polluted wells in Virginia have been reported.

Average dietary iodine intake has been estimated both from dietary studies and from analysis of thyroidal radioiodine uptakes by the thyroid. Oddie *et al.* (1970) studied radioiodine uptakes that were reported by 133 observers from approximately 30,000 euthyroid subjects throughout the United States. These estimates indicated that daily iodine intakes in various sections of the country varied from approximately 240 to 740 μg/day.

Requirements

The Recommended Dietary Allowances (RDA's) for the intake of iodine by adults range from 0.08 to 0.140 mg/day, depending upon age and sex (NAS, 1974c). The full list of recommendations is shown in the overall summary section at the end of this report. An intake of less than 0.05 mg/day leads to endemic goiter (NAS, 1974a).

Toxicity versus Essential Levels

Both iodine deficiency and excess can enlarge the thyroid, a condition termed goiter. Endemic goiter due to iodine deficiency, which was prevalent in the United States before salt was iodized, is now uncommon. A reduction in the incidence of endemic goiter may also be due in part to the use of breads containing iodate. Measurement of the urinary excretion of iodine suggests that moderate iodine deficiency still occurs in the United States. In the

National Nutrition Survey conducted from 1968 to 1969, only a small percentage of persons sampled had visibly enlarged thyroid glands. For example, McGanity (1970) reported that 5.4% of the individuals examined in one study in Texas had palpable or visibly enlarged thyroid glands. Eleven individuals, or approximately 0.4% of this sample, had urinary iodine levels of less than 50 µg/g creatinine, but none of their thyroids were enlarged. However, 9% of those whose iodine excretion was less than 100 µg did have enlarged thyroid glands (Matovinovic, 1970).

In the 1968-1969 Texas nutrition survey (McGanity, 1970), there was no evidence that the iodine content of drinking water was related to the incidence of enlarged thyroid. Furthermore, there was no relationship between the incidence of enlarged thyroid and the fluoride content or hardness of water.

In a study that was conducted in Virginia, Vought et al. (1967) reported that thyroid disease in children is not related to dietary iodine deficiency, but rather to contaminated water. They isolated cultures of microorganisms from contaminated waters and postulated that goitrogens known to be produced by these organisms might interfer with iodine uptake by the thyroids of the affected children.

Plant goitrogens have been implicated as a factor contributing to endemic goiter in many parts of the world, particularly in areas such as the Congo, where there is also dietary iodine deficiency (Delange and Ermans, 1971). While there is no evidence that plant goitrogens play a role in the production of enlarged thyroid or thyroid disease in the United States, too little is known about the possible effects of low doses of goitrogens on the availability of iodine to the neonate or to the developing fetus (Stanbury, 1970). During pregnancy iodine deficiency can impair the development of the fetal thyroid thereby producing cretinism. Endemic cretinism does not occur in the United States.

Goiters resulting from iodine overload have been well described in the United States and other countries. Although goiters can be produced by excessive dietary iodine intakes, the more common cause is ingestion of large quantities of iodine-containing medications. Wolff (1969) has divided iodine goiter into four groups: 1) adult iodine goiter, mostly in asthmatic subjects taking iodine-containing cough medicines; 2) iodine goiter of the neonate due to placental transfer of iodide from mothers who are being treated with iodide; 3) endemic iodine goiter, which is of dietary origin; and 4) hypothyroidism in patients with thyrotoxicosis (Graves diseases) who are being treated with potassium iodide (KI) or Lugol's solution (4.5-5.5 g of iodine and 9.5-10.5 g of potassium iodide per 100 l of purified water). Most people who have developed iodine goiter have received very large amounts of iodine for prolonged periods. In iodine goiter cases reviewed by

Wolff, intakes of iodine ranged from 18 mg to more than 1 g/day over several months. When iodine goiter develops under these conditions, a secondary complication may be hypothyroidism with clinical signs of myxedema. Prenatal development of iodide goiter carries the risk of obstructed delivery or neonatal tracheal obstruction. According to Wolff, there is a danger of iodine goiter from prolonged intakes of iodine above 1-2 mg/day.

In Northern Tasmania, two waves of increased prevalence of thyrotoxicosis have been attributed to iodine excess. In 1964, the incidence of thyrotoxicosis in Northern Tasmania increased. This was attributed to the use of iodophor disinfectants on dairy farms which, as previously stated, causes iodine residues to be present in milk. In 1966, another epidemic of iodine-induced thyrotoxicosis occurred in the same country. This time it was precipitated by the addition of iodate to bread to prevent endemic goiter (Stewart and Vidor, 1976).

Liewendahl and Gordon (1974) reported a case of iodide goiter in a woman who ingested seaweed for 2 years. Hyperthyroidism also occurred in this patient.

Stanbury (1970) cited an unpublished report of a study in Iceland, where the iodide intake is high (from 0.500-1.500 mg/day) because of the prevalence of fish in the diet. The investigator also reported that the incidence of papillary carcinoma of the thyroid was high in Iceland. In parts of Japan, where large intakes of iodine result from the local custom of eating seaweed, carcinoma of the thyroid is more prevalent than in any other country (Suzuki et al., 1965). It has been suggested that the persons at risk of thyroid carcinoma from high iodine intake are those with preexisting thyroid adenoma or goiter.

Furszyfer et al. (1970) called attention to a rise in the prevalence of subacute (granulomatous) thyroiditis in Olmstead County, Minnesota between 1960 and 1967. In a subsequent study (Furszyfer et al., 1972), they reported that the prevalence of Hashimoto's disease (lymphomatoid thyroiditis) in Rochester, Minnesota had increased from 6.5 per 100,000 females during 1935-1944 to 69.0 during 1965-1967. They suggested a relationship to excess iodine intake.

Iodide may produce acneiform skin eruptions. Sources of iodine cited as being responsible for production of iododermas are iodized salt, iodides in therapeutic vitamin-mineral preparations, and iodine in formula foods such as Metrecal.

Anaphylactic reactions as well as acneiform eruptions and furunculosis (boils) may follow intravenous administration of iodide preparations used as contrast substances for intravenous pyelograms and gall bladder or spinal X-rays (Baer and Witten, 1961).

Interactions

Lead has an adverse effect on the uptake of iodine by the thyroid gland. Persons with lead-poisoning from industrial exposure or from ingestion of lead-contaminated, illicitly distilled whiskey have developed impairment of iodine uptake by the thyroid (Sandstead, 1977).

Contributions of Drinking Water to Iodine Nutrition

Contributions of Drinking Water to Iodine Requirements

Assuming a 2 l/day consumption of drinking water and total iodine requirements in the range of 0.080 to .0150 mg/day, low iodine waters (approximately 0.001 mg of iodine per liter) would provide 1%-2% of the total requirement, medium iodine waters (0.004 mg/l), 5%-10%, and high (polluted) iodine waters (0.018 mg/l), 24%-44%.

Contributions of Drinking Water to Total Intake

Given the highest level of iodine in water at 0.018 mg/l and a total intake of iodine equivalent to 0.240 mg/day, the contribution of water (2 l/day) would be approximately 15%. Minimal contributions to total body burden would be made by low iodine waters if high iodine intakes from food were consumed (at a level of 0.740 mg/day). Under these conditions, iodine would contribute 0.3% to total intake. Where dietary intake of iodine is low and drinking water is obtained from polluted wells with high iodine content, the water could contribute to the prevention of iodine deficiency. However, in view of Vought's findings of bacterial goitrogens in polluted water (Vought _et al_., 1970), this seems unlikely. Iodine toxicity is unlikely to be related to water intake unless water was highly contaminated with iodine.

Conclusions

Table 10 summarizes information on iodine in drinking water and the diet. The average intake of iodine from all soruces appears to be at least twice the RDA. Reduction of iodine intake to approximate the RDA is desirable. In some cases, reduction of the level in water would contribute to reduction of intake, but reduction of intake from other sources may be more practical.

Research Recommendations

Further data should be obtained on the iodine content of water supplies.

Microbiological examination of high iodide waters for fecal and urinary contamination should be performed.

Methods for the reduction in the iodide content of high iodine waters should be investigated.

TABLE 10

Contribution of Drinking Water to Requirements for Iodine, Sodium, and Potassium (Values Based on a 70 kg Adult Man and Water Intake of 2 l/day)[a]

Requirements	Sodium	Potassium	Iodine
Requirement per day, mg[b]	2,500	2,500	0.130
Ratio of toxic intake level to dietary requirement			
acute[a]	4.7	2.2	
chronic[c]	5.5	unknown	7.7
Mean Concentrations			
Mean concentration in water, mg/l	27.7	2.15	0.004
Intake based on mean concentration in water, mg/2 l	55.4	4.3	0.008
Intake from water based on mean, % of Requirement	2.0	2.0	6.0
Highest Concentrations Observed			
Highest concentration in water, mg/l	79.7	8.3	0.018
Intake based on highest observed concentration in water, mg/2 l	159.4	16.6	0.036
Intake from water based on highest observed concentration, % of Requirement	6.0	7.0	28

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[a] References to the data in this table will be found in the text. Data available on chloride were not considered sufficient for compiling an assessment for that nutrient.

[b] These are intermediate values, selected for illustrative purposes, from the Recommended Dietary Allowances (NAS, 1974;NAS, in press)

[c] Toxicity is expressed in terms of the ratio of intake to requirement which, over the long-term, causes mild to severe signs of toxicity (FDA, 1975).

Changes in total iodine intake over time by the U.S. population should be studied by monitoring individual foods and total "market-basket" samples.

Extraneous sources of iodine due to air and water pollution, use of iodophors, use of erythrosine, and use in vitamin-mineral preparations should be reduced.

The relationships between acne and acneiform eruptions and iodine intake from water as well as food or other sources such as medication should be examined.

IRON

Throughout the world, including the United States, iron deficiency is one of the most commonly recognized signs of inadequate nutrition. This situation exists in spite of the fact that iron is among the most abundant elements in the earth's crust. There are several reasons for the anomaly. Man has developed an effective mechanism to prevent excess absorption of iron. This protective device is important because iron is poorly excreted and is highly toxic when tissue levels rise above the tolerance level. Iron compounds tend to be insoluble and the iron of such compounds is inefficiently absorbed. Thus, while the quantity of iron consumed is important, the chemical form of the iron is also a highly significant factor in meeting the dietary requirement. In view of these considerations it is understandably difficult to assess the dietary iron requirement of humans.

Presence in Food, Water, and Air

The concentration of iron in foods consumed by humans varies widely, ranging from less than 1 mg/kg in milk and related products to approximately 50 mg/kg in dry beans and cereals. See Table 11 (at the end of the section on zinc) for a tabulation of data on the amount of iron contained in food groups and the percentage of the mineral contributed by the food groups to the total food intake of persons in U.S.

households (unpublished data, Consumer and Food Economics Institute, Science and Education Administration, U.S. Department of Agriculture). Approximately 35% of the dietary iron comes from meat, fish, and eggs, while 50% is supplied by cereals, root vegetables, and other foods of plant origin.

The median iron concentration in surface air layers at 38 U.S. nonurban sites was 0.255 μg/m³ (NAS, 1979). Twenty cubic meters of such air (the average volume inhaled per day) would contain approximately 5 μg of iron. Even if totally absorbed, this quantity would make a negligible contribution to the daily intake of iron.

An estimate of the iron content of drinking water and its contribution to the iron requirement of the U.S. population are given in Table 12. While the concentrations of iron in raw water and wastewaters are highly variable and, in some cases, quite high, this report is concerned only with finished water, most particularly, with tap water. Of 672 water samples collected from interstate carriers (suppliers) of water and analyzed for the U.S. Environmental Protection Agency (USEPA, 1975), 62.5% contained iron concentrations that could be estimated quantitatively. The average concentration in these 420 water samples was 0.240 mg/l. The samples were collected from 10 regions in the continental United States. The mean of the maximum values was 2.180 mg/l. In another EPA study (Craun _et al_., 1977; Greathouse _et al_., 1979), tap water samples from 3,834 residences in 35 regions of the United States were analyzed. The mean and maximum concentrations of iron in these samples were 0.245 and 2.180 mg/l, respectively.

Requirements

The requirement for most nutrients, including iron, varies with the age and physiological state of the individual, but the difference between the male and female requirement for iron is greater than for most nutrients. This stems largely from the blood loss of females during the reproductive period and the increased demand during pregnancy.

Iron is inefficiently absorbed. Consequently, to meet the actual daily requirement for absorbed iron (approximately 1.0 mg for males and 1.5 mg for females), from 10 to 20 times that quantity must be ingested. The percentage of iron absorbed depends on the iron status of the individual, i.e., absorption is greater in persons with iron depletion. There are also differences in availabilities among the various iron compounds in the diet. To assure adequate intake for the majority of the population, the recommended dietary allowance (RDA) (NAS, 1974) is 10 mg for adult males and 18 mg for females of reproductive age. See Table 12 at the end of the section on zinc for requirements and toxicity of iron compared to similar information for copper and zinc.

Toxicity versus Essential Levels

When administered parenterally, iron is a highly toxic element. Humans are generally well protected from oral overdose, but children from 1 to 2 years of age are particularly vulnerable to iron toxicity from ingestion of iron supplements that have been commercially prepared for adults (Fairbanks et al., 1971). In general, the long-term toxic levels of dietary iron for monogastric animals is 340 to 1,700 times greater than the requirement. Such continuous intake may give rise to signs of toxicity (FDA, 1975).

Interactions

The bioavailability of iron in foods varies widely. For example, iron in the form of heme is absorbed nearly 10 times as efficiently as iron in food of plant origin. Practically nothing is known about the absorption of iron from water. As a matter of fact, little is known about the chemical species of iron from drinking water at the tap. In a well-aerated river the dominant form is ferric iron (Fe^{+3}). Groundwater may contain appreciable ferrous iron (Fe^{+2}). Surface and groundwaters also contain organic complexes of iron (NAS, 1979). The fractions of these forms in water that are absorbed by humans are unknown, but it is clear that reducing agents, such as ascorbic acid, increase the absorption of iron in food (Monsen et al., 1978).

Ferrous iron appears to have better bioavailability than does ferric iron. The iron in certain chelates, such as ferric phytate, is poorly absorbed (Bowering _et al_., 1976). Although it is generally assumed that trace elements in water are readily absorbed, there are few, if any, data relative to the bioavailability of iron in water.

Iron interacts physiologically with several nutritionally essential and nonessential elements. All of these elements, including copper, zinc, manganese, and lead, tend to increase the requirement for iron. Signs of copper toxicosis are eliminated by the addition of extra iron and zinc to the diet, and signs of zinc toxicosis are prevented by the addition of extra copper and iron (Magee and Matrone, 1960). The signs of lead toxicity are exacerbated by iron deficiency. Perhaps the most significant interaction of any mineral with iron is that of manganese. Excess manganese impairs hemoglobin regeneration by decreasing the absorption of iron (Underwood, 1977). (See the section on manganese for further discussion of the iron-manganese interaction.)

Contributions of Drinking Water to Iron Nutrition

Assuming a 2 l/day consumption of water containing an iron concentration equal to the mean value shown in Table 12, water would contribute approximately 0.5 mg of iron, which is about 5% of the male requirement and less than 3% of the female requirement. For those persons consuming water containing the highest observed value, water would contribute from 17 to 44% of the daily requirement, depending on sex.

Conclusions

In the continental United States, most tap water probably supplies less than 5% of the dietary requirement for iron. This may be considered a negligible contribution unless the iron in water has an appreciably higher bioavailability than iron in food. However, iron deficiency is common in the United States. Under severely limiting conditions, 0.5 mg of highly available iron from water would make a significant contribution to the daily dietary intake. If a local water supply contained unusually high concentations of iron, it could contribute substantially to the total intake. The iron content of drinking water should not be reduced since there is little or no likelihood of toxicity from iron in natural foods and water. It should be noted that the present recommended limit for iron in water, 0.3 mg/l, was based on taste and appearance rather than on any detrimental physiological effect from iron in water.

Research Recommendations

The chemical species of iron in drinking water and their bioavailability should be determined.

COPPER

While there is no evidence of copper deficiency in the U.S. population, except for isolated cases in patients maintained by total parenteral nutrition, copper is clearly an essential nutrient. There is some evidence that the intake is lower than required for optimal human nutrition. Klevay (1975) suggested that borderline deficiencies may occur among portions of the population. The concentration of copper in the earth's crust is estimated to be 50 mg/kg. It forms organic complexes readily and tends to concentrate in clay minerals, particularly in clays that are rich in organic matter. Copper in rocks is mobilized more readily under acidic rather than alkaline conditions (NAS, 1977). The species of copper in drinking water at the tap have not been determined, but copper presumably occurs in the oxidized, Cu(II) state complexed with various ligands. The reaction of soft water with the copper pipes that are used in some household plumbing systems contributes to the copper levels in water at the tap (Schroeder et al., 1966).

Occurrence of Copper in Food and Water

The concentrations of copper in foods is highly variable. They are extremely low in dairy products and relatively high in cereals and roots. Table 11 (at the end of the section on zinc) shows the distribution of copper among food groups. These data suggest that the average copper intake is less than 2 mg per day. Klevay (1975) has presented evidence that many U.S. diets contain much less copper than required. For example, he quotes studies showing that the dietary copper intake of high-school girls and college women may be as low as 0.34-0.58 mg and that the diets of other individuals may supply less than 1 mg/day.

The estimated contribution of drinking water to an adult's copper requirement is shown in Table 12 (in the section on zinc). Because the concentration of copper in drinking water is highly variable, means are of limited significance. Approximately 55% of the 604 water samples analyzed by the EPA (USEPA, 1975) contained measurable levels of copper. The mean of these samples was 60 μg/l. The mean of another study (Craun et al., 1977; Greathouse et al., 1979) was 150 μg/l.

Requirements

Signs of copper deficiency have been observed in patients maintained totally by intravenous alimentation, but there is only one report of copper deficiency in children fed natural food by mouth (Meng, 1977). Since signs of dietary copper deficiency in the United States have not been observed among persons consuming commonly available foods, it has been assumed that the usual intake meets the requirement. The NAS Food and Nutrition Board has not previously set an RDA for copper, but has recently estimated an adequate and safe intake of 2 to 3 mg/day (see Table 31:

NAS, in press). Copper intakes between 1.3 to 2 mg have been shown to maintain nutritional balance in preadolescent girls and adults of both sexes (NAS, 1974).

Toxicity versus Essential Levels

Copper is toxic to monogastric animals when ingested in quantities that are 40 to 135 times greater than their respective requirements (FDA, 1975). Except for sheep, all animals absorb copper poorly because their gastrointestinal tracts provide an excellent barrier against oral toxicity. The greatest danger of toxicity arises when children consume acidic beverages that have been in contact with copper containers or valves (FDA, 1975). The interim drinking water standard (USEPA, 1977) of 1 mg/l is based on taste rather than toxicity and affords adequate protection to the general public. However, a few Wilson's disease (hepatolenticular degeneration) patients are adversely affected by the estimated average intake of copper (Scheinberg and Sternlieb, 1965).

Interactions and Bioavailability

Copper probably occurs in drinking water in the form of the cupric ion (Cu^{+2}) complexed with organic ligands, but this has not been determined. It is reasonable to assume that it is as biologically available as the copper in food, if not more so. High levels of ascorbic acid adversely affect the absorption and metabolism of copper, but few other organic dietary constituents are known to affect its bioavailability (Carlton and Henderson, 1965; Hill and Starcher, 1965; Hunt et al., 1970).

The interaction of two essential trace elements with copper increases the requirement of humans for copper. For example, high levels of zinc exacerbate the signs of copper deficiency in mammals. This effect can be reversed by feeding extra copper to the subject (O'Dell et al., 1976). The antagonism of molybdenum to copper is augmented by sulfate (SO_4). This interaction is particularly significant in ruminant animals but may be of little importance in humans. Copper, sulfur, and molybdenum form an insoluble copper thiomolybdate complex (Dick et al., 1975). Silver and cadmium, both nonessential elements, also interact with copper to exacerbate signs of deficiency (Underwood, 1977).

The Contribution of Drinking Water to Copper Nutrition

If one assumes a typical concentration of copper in drinking water of 0.1 mg/l, a human would obtain 0.2 mg of copper from 2 liters of water. This constitutes between 6.0% and 10% of the estimated adequate and safe intake. In view of the data assembled in Table 11, indicating that the typical copper intake from food is less than 2 mg/day, and other observations (Klevay, 1975) suggesting even lower consumption of copper from food, the contribution of water to total copper intake becomes even more significant.

Furthermore, some drinking water contains considerably higher levels of copper than 0.1 mg/l and would contribute a correspondingly greater proportion of the total intake. Waters containing the average reported maximum copper concentrations would supply approximately 40% of the requirement. Although overt signs of copper deficiency have not been reported in enterally nourished persons in the United States, the margin of safety may not be large and the contribution of drinking water to copper nutrition should not be overlooked.

Conclusions

Table 12 (in the section on zinc) provides a summary of information on the requirement for copper and its intake from various sources. Under present circumstances, copper deficiency in the typical U.S. diet is unlikely, but the total intake may be borderline in some sections of the population. Based on average food and water concentrations, most drinking water contributes a small proportion of the daily copper intake. Nevertheless, the extra copper contributed by water is a dietary safety factor which should be maintained if feasible. The potential for toxicity from the levels of copper in drinking water is extremely low.

Research Recommendations

The species of the copper in drinking water and its bioavailability should be determined.

ZINC

The importance of zinc to human nutrition has been recognized since 1962 when overt zinc deficiency was observed among rural inhabitants of the Middle East (Prasad et al., 1963). There is also evidence of zinc deficiency among U.S. children who were not suspected of being nutritionally deprived (Hambidge and Walravens, 1976). These observations came as a surprise inasmuch as zinc is ubiquitous in food, water, and the general environment. This anomaly is explained in part by the low bioavailability of zinc in many foods, particularly plant seeds. The zinc ion (Zn^{+2}) forms strong chelates with many ligands, and it occurs commonly in nature in the form of complexes. The zinc in some of these complexes is readily absorbed, but in others, it is poorly absorbed (O'Dell, 1969). Unfortunately, the species and bioavailability of zinc in drinking water are unknown.

Presence in Food, Water, and Air

Zinc is widespread in commonly consumed foods, but tends to be higher in those of animal origin, particularly some seafoods (see Table 11 at the end of this section). Furthermore, the zinc in foods of animal origin has a higher bioavailability than zinc in foods of plant origin. Unless foods are carefully selected, it is difficult to meet the 15 mg/day recommended dietary allowance (RDA) with an intake of 2.0 kilocalories or less.

The zinc concentration in U.S. urban air is generally less than 1 μg/m³. Assuming that 20 m³ of air is inhaled per day (NAS, 1979), air contributes less than 20 μg of zinc to the daily intake of adults.

Of the 583 water samples analyzed by the EPA (USEPA, 1975), 67% had detectable levels of zinc. The mean concentration in these 392 samples was 100 μg/l, compared to 245 μg/l observed in another study (Craun et al., 1977; Greathouse et al., 1979).

Requirements

The NAS Food and Nutrition Board (NAS, 1974) has set the adult requirement for zinc at 15 mg/day. Although this may be higher than the actual requirement under many circumstances, it is designed to meet most needs under all conditions of bioavailability.

Toxicity versus Essential Levels

The absorption of zinc is poorly understood, but appears to be well-regulated. It is affected by such factors as the body's requirement for zinc as well as by the presence of chelating agents, e.g., phytates. Consequently, zinc has low toxicity when taken orally (Evans, 1976). As shown in Table 12, there is a wide range of ratios (40-280) of toxic levels and requirements for zinc in the diets of monogastric animals. The greatest potential for zinc toxicity occurs when dietary copper is deficient or limited. Since copper deficiency is improbable in U.S. diets, zinc toxicity from food is highly unlikely.

The interim drinking water standard, 5 mg/l (USEPA, 1977), is based on taste and appearance of the water rather than on toxicity. Considering the relatively low intake of zinc in food, this standard provides a wide margin of safety.

Interaction and Bioavailability

The bioavailability of zinc in foods varies widely. Phytate, a common constitutent of plant seeds, binds zinc strongly and decreases its absorption (O'Dell, 1969). Excess calcium in the presence of phytate accentuates the effect of the phytate. Dietary fiber also decreases the absorption of zinc along with that of other nutrients studied (Reinhold _et_ _al_., 1976).

Cadmium is closely related to zinc in its electronic configuration, and the two ions interact physiologically. Cadmium tends to increase the requirement for zinc or, stated in another way, zinc decreases the toxicity of cadmium (Underwood, 1977). Whereas calcium decreases the bioavailability of zinc in the presence of phytate, there is little evidence for a major direct calcium-zinc interaction. There is a copper-zinc interaction, which is described in the section on copper. Excess zinc exacerbates copper deficiency, but there is no evidence that excess copper aggravates zinc deficiency.

The Contribution of Drinking Water to Zinc Nutrition

If one assumes a mean concentration of 200 µg/l, drinking water would supply 0.4 mg or approximately 3% of the daily requirement. Under most circumstances this is a negligible contribution to the total intake. However, in view of the potential for zinc deficiency in the U.S. population, even 0.4 mg should not be ignored. Some drinking water contains much higher concentrations of zinc than the mean value. The highest observed water concentrations might contribute up to 20% of the daily human requirement.

Conclusions

Zinc is an essential nutrient for humans. There is evidence of borderline deficiencies of the element in children in the United States as well as in other parts of the world (Hambidge and Walrens, 1976). Normally, drinking water contributes less than 5% of the dietary requirement. From that standpoint, it may be considered insignificant. However, in view of possible deficiency in U.S. diets, it is prudent to maintain all dietary sources of zinc, even those as small as 0.5 mg/day.

The possibility of detrimental health effects arising from zinc consumed in food and drinking water is extremely remote.

Research Recommendation

The chemical form and bioavailability of zinc in water should be determined in order to evaluate the contribution of water to the requirement for zinc.

TABLE 11

Iron, Copper, and Zinc in U.S. Diets [a]

Food Group	Content per kg of food as purchased [b]			Mineral Contributed to Diet by Food Group					
				Amount per person per day			Percentage of total food intake [c]		
	Iron, mg	Copper, mg	Zinc, mg	Iron, mg	Copper, mg	Zinc, mg	Iron, %	Copper, %	Zinc, %
Milk, cheese, ice cream [d]	0.4	0.10	4.3	0.3	0.06	2.5	2	4	20
Meat, poultry, fish	20.1	.49	18.6	5.9	.14	5.5	31	10	43
Dried beans, and peas, nuts [e]	46.3	7.17	24.7	.9	.13	.5	5	9	4
Eggs	20.5	.89	12.7	1.0	.04	.6	5	3	5
Vegetables, dark-green and deep-yellow	9.5	.88	2.8	.3	.03	.1	2	2	1
Citrus fruit, tomatoes	4.2	.54	1.8	.7	.09	.3	4	6	2
Potatoes	5.7	1.80	2.4	.6	.19	.3	3	13	2
Other vegetables, fruit	5.7	.70	2.0	2.0	.25	.7	10	17	6
Cereal, pasta	54.7	2.26	16.3	2.8	.12	.8	15	8	7
Flour, mixes	25.4	2.26	2.8	1.1	.09	.1	6	6	1
Bread	24.0	1.61	7.2	2.0	.14	.6	10	10	5
Other bakery products	11.0	1.26	6.0	.8	.09	.4	4	6	3
Fats, oils	.7	.64	1.8	0	.03	.1	0	2	1
Sugar, sweets	7.9	.88	.6	.6	.06	0	3	4	0
TOTAL FOOD				19.0	1.46	12.5	100	100	100

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[a] Unpublished data from the Consumer and Food Economics Institute, Science and Education Administration, U.S. Department of Agriculture, Hyattsville, MD 20782, January 1979. Food as purchased or brought into the kitchen from garden or farm except as noted. Mineral content of diet is estimated for the edible portion of food as purchased and does not allow for losses due to discarding of edible food during preparation and consumption in the home. Also, the mineral content of the diet and the contribution of food groups in any person's diet may differ considerably from those shown, depending on kinds and amounts of foods consumed.

[b] Estimates for copper and zinc are based on a limited number of analyses.

[c] Excludes alcoholic beverages; nonalcohlic beverages, such as coffee, tea, cocoa, soft drinks, punches, and ades; seasonings; and leavening agents.

[d] Quantity is in terms of whole fluid milk to which dairy products, except butter, are equivalent in calcium content.

[e] Quantity is in terms of dry beans and peas, shelled nuts, and peanut butter.

TABLE 12

Contribution of Drinking Water to the Dietary Requirements for Iron, Copper, and Zinc

Ranges of Values Based on 70-kg Adult Human	Iron	Copper	Zinc
Requirement,[a] mg/day	♂ 10 : ♀ 18	2-3	15
Ratios of toxic intake levels[b] to dietary requirement	340-1,700	40-135	40-280
Likely concentrations in water,[c] µg/l	240-245*	60-150*	100-245*
Daily intake based on likely concentrations in water, mg/2 l	0.48-0.49	0.12-0.30	0.20-0.49
Likely water contributions to requirement, %	2.7-4.9	4-15	1.3-3.3
Highest concentrations[d] observed in water, µg/l	1,560*-2,180	440*-450	1,320*-1,490
Daily intake based on highest observed concentrations in water, mg/2 l	3.1-4.4	0.88-0.90	2.6-3.0
Water contribution to requirement based on highest observed concentration in water, %	17-44	30-45	17-20

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[a] These are Recommended Dietary Allowances (NAS, 1974) except the values for copper, which are estimated as adequate and safe intakes (NAS, in press).

[b] Toxic levels for monogastric animals that cause mild to severe signs of toxicity over the long term (Food and Drug Administration, 1975). Expressed as ratios of toxic levels to dietary requirements.

[c] The likely concentrations are based on analytical data from two sources; USEPA (1975) report on interstate carrier water supplies and the study reported by Craun _et al_. (1977) and Greathouse _et al_. (1979). * = the values derived from the Craun and Greathouse study. In the USEPA study (1975), 672 samples from 10 regions were analyzed for iron. Analytical values were reported for 62.5% of the samples. The mean is based on these values. Of the 604 samples that were analyzed for copper, 55% contained sufficient copper to report. These were averaged. Of the 583 samples analyzed for zinc, 67% were averaged.

[d] The maximum values reported by Craun _et al_. (1977) and Greathouse _et al_. (1979) are marked with an asterisk. The other values are the means of the maximum values found in the 10 regions sampled by the USEPA.

SELENIUM

Presence in Food, Water, and Air

The amount of selenium in different foods is highly variable, depending upon where the plants were grown or where the animals were raised. There are great differences among the selenium contents of soils and, thus, the amount that is available for uptake by plants. This selenium is passed directly up the food chain through the plants to animals and humans. There are areas of the United States and other parts of the world where the selenium content of soil is either so low or so high that naturally occurring deficiencies or toxicities of selenium can occur in animals.

The estimated human daily intake of selenium from dietary sources tends to reflect the amount of selenium that is available in the soils (Table 13). For example, in New Zealand, where the selenium contents of soils are low, the daily dietary intake of selenium is only 56 µg/day, whereas in Venezuela, where soils contain high selenium concentrations, the intake is 326 µg/day. Daily dietary intakes of selenium by humans range from 24 µg in certain diets in New Zealand (Stewart *et al.*, 1978) to 7,000 µg in highly seleniferous diets in South Dakota (Smith and Westfall, 1937).

Less than 0.5% of the samples taken from various public water supply systems in the United States exceeded the USEPA (1975) limit for selenium, 0.01 mg/l (Lakin and Davidson,

TABLE 13

Estimated Daily Intake of Selenium by Humans from Dietary Sources

Food	Estimated Intake by Country, ug/day										
	New Zealand[a]	Japan[b]	Toronto(1), Canada[c]	Maryland, USA[a]	Toronto(2), Canada[c]	Canada[a]	"Market-Basket Survey, USA"[d]	Winnipeg, Canada[a]	S. Dakota USA[e]	Halifax, Canada[c]	Caracas, Venezeula[f]
Vegetables, fruit, sugars	6	7	5	5	1	7	2	9	10	7	15
Cereals	4	24	62	45	112	74	103	80	57	105	88
Dairy products	8	2	7	14	5	23	5	28	48	22	70
Meat, fish	38	56	25	69	30	46	59	64	101	90	153
TOTALS	56	88	98	132	149	151	169	181	216	224	326

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[a] Data from Watkinson, 1974. Intake estimates based on analyses of separate foods.

[b] Data from Sakurai and Tsuchiya, 1975. Intake estimates based on analyses of separate foods.

[c] Data from Thompson et al., 1975. Intake estimates based on food composite data.

[d] Data from McLoughlin, J.H., personal communication. Estimated intake by adults consuming 3900 Calories/day based on food composite from fiscal year 1974 Total Diet Survey of the U.S. Food and Drug Administration ("Market-Basket Survey").

[e] Data from Olson et al., 1978. Intake estimates based on analyses of separate foods.

[f] Data from Mondragon and Jaffe, 1976. Intake estimates based on analyses of separate foods, but assuming a food consumption pattern more typical of North America.

1967; McCabe et al., 1970; Taylor, 1963). Although there are exceptions, especially in areas where there are high levels of selenium in the soil, the NAS Committee on Medical and Biologic Effects of Environmental Pollutants (MBEEP) concluded that "waters rarely contain selenium at levels above a few micrograms per liter. Hence, they can rarely be considered a significant source of the element from either a nutritional or a toxicity standpoint" (NAS, 1976). This statement is confirmed by other analytical data from the United States and by some from Europe as well (Table 14). Even if it is assumed that a person drinks 2 l of water per day containing the EPA limit, the average daily intake of selenium via water would be only 20 μg. In most countries, this is still a small fraction of the selenium that is consumed in foods.

Zoller and Reamer (1976) reported that the atmospheric concentrations of selenium in most urban regions range from 0.1 to 10 ng/m³. Hashimoto and Winchester (1967) and Pillay et al. (1971) measured concentrations of selenium in air at 0.3 to 1.6 ng/m³ and 3.6 to 9.7 ng/m³, respectively. The NAS MBEEP Committee concluded that the amount of airborne selenium is very small, probably well below 10 ng/m³ (NAS, 1976). Assuming that a typical person ventilates 20 m³ of air daily and that ambient air concentrations of selenium are not likely to exceed 10 ng/m³, the maximum daily intake via this route would be only 0.2 μg, which is much less than that derived from foods. Therefore, it can be concluded

TABLE 14

Concentration of Selenium in Drinking Water

Mean Selenium Concentration, and Range, µg /l	Description of Sample	Comment	Reference
0.6 (range, 0.2 to 2.4)	Public water supplies from five European cities	Four of five samples contained <1 µg/l	Zoeteman and Brinkmann, 1977
0.36 (range, 0.08 to 0.9)	Tap water from three Swedish cities		Boström and Wester, 1967
3.5 (range, 1.0 to 6.5)	4,200 tap water samples from throughout the United States	Represents less than 10% of all samples; more than 90% were below the detection limit of the analytical method used (1 µg/l)	Greathouse and Craun, 1978

that air contributes insignificantly to the average daily intake of selenium by the general population.

Distribution in Tissues

Schroeder _et al_. (1970) analyzed from two to six samples each of various human tissues obtained at autopsy. They found that the kidney and liver contained the highest concentrations of selenium (Table 15). Other tissues containing selenium, in order of decreasing concentrations were: spleen, pancreas, testes, heart, muscle, and small intestine. The lungs and brain contained the lowest concentrations of selenium.

They calculated the total body content of selenium in subjects from the United States to be 14.6 mg (range, 13.0 to 20.3 mg) for 91.7% of the body. Stewart _et al_. (1978) estimated the total body selenium content in New Zealanders to be either 6.1 mg (range, 4 to 10 mg) or 3.0 mg (range, 2 to 5 mg) depending on whether selenomethionine $[CH_3Se(CH_2)_2CH(NH_2)COOH]$ or selenite (SeO_3^{2-}) was used in the estimation.

Requirements

The critical level of dietary selenium below which deficiency symptoms are observed is generally considered to be approximately 0.02 mg/kg of feed for ruminants and 0.03 to 0.05 mg/kg for poultry (NAS, 1971). A nutritionally

TABLE 15

Selenium Content of Certain Human Tissues[a]

Tissue	Number of Samples	Mean Selenium Content and Range, mg/kg Wet Tissue
Kidney	6	1.09 (0.61-1.84)
Liver	6	0.54 (0.28-0.81)
Spleen	4	0.34 (0.28-0.47)
Pancreas	3	0.30 (0.27-0.34)
Testes	3	0.30 (0.15-0.38)
Heart	5	0.28 (0.25-0.37)
Muscle	5	0.24 (0.11-0.38)
Small intestine	3	0.21 (0.12-0.32)
Lung	6	0.16 (0.06-0.26)
Brain	2	0.13 (0.04-0.21)

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[a] Adapted from Schroeder _et al_., 1970

generous level of dietary selenium is 0.1 mg/kg for livestock and 0.2 mg/kg for poultry. For a 70-kg human consuming 1 kg of diet per day (dry basis), this would translate into a daily intake of 100 to 200 μg. An estimated adequate and safe intake of selenium for adult humans has been suggested to be between 50 and 200 μg with correspondingly lower intakes for children and infants (NAS, in press; see Table 3T in the Summary of this report). Any daily intake within the recommended ranges shown in the table is considered adequate and safe, but the recommendations do not imply that intakes at the upper limit of the range are more desirable or beneficial than those at the lower limit. Stewart et al. (1978) have recently indicated that the minimum dietary requirement of selenium for the maintenance of normal human health is probably not more than 20 μg/day.

Toxicity versus Essential Levels

Several studies indicate that diets containing 5 mg/kg of selenium or more cause chronic toxicity in laboratory animals (see review by Moxon and Rhian, 1943). In seleniferous areas, 5 mg/kg of diet is generally accepted as the dividing line between toxic and nontoxic feeds (NAS, 1976). If 5 mg/kg is accepted as the dietary toxic level of selenium and 0.05 mg/kg is considered to be the dietary critical minimum for protecting against selenium deficiency, then the ratio between the toxic and beneficial doses is

100, a value not too different for many other minerals and nutrients.

On the other hand, some investigators have claimed to find toxic effects of selenium in rats fed diets containing less than 5 mg/kg under certain conditions (Table 16). For example, Witting and Horwitt (1964) showed that 1 mg/kg of dietary selenium depressed growth in vitamin-E-deficient rats. Harr _et al_. (1967) reported that the addition of 0.5 mg/kg of selenium to a semipurified diet caused proliferation of the hepatic parenchyma. But these liver changes were observed to an even greater extent in rats fed a commercial diet not supplemented with selenium. Therefore, the relationship between the liver lesions and selenium intake is not clear.

Pletnikova (1970) administered selenium to rats in drinking water in doses that were roughly equivalent to a dietary selenium intake of 0.06 mg/kg. Such doses appeared to cause decreased blood glutathione levels, impaired liver function, depressed hepatic succinic dehydrogenase activity, and certain modifications in behavior. Since this level of selenium intake is similar to that needed to prevent selenium deficiency in animals, the toxicological significance of these observations is not clear unless a specific level of selenium in drinking water is more deleterious than an equivalent dose in the diet. However, there have been few studies in which the toxicity of selenium given in these two ways has been compared directly.

TABLE 16

Toxicity of Selenium in Rats

Experimental Conditions	Criteria of Toxicity	Dose of Dietary Selenium Causing Effect, mg/kg	Reference
Normal diet	Growth inhibition	4 to 5	NAS, 1976
Vitamin-E-deficient diet	Growth inhibition	1	Witting and Horwitt, 1964
Semipurified diet	Liver lesions	0.5	Harr *et al*., 1967
Selenium given in drinking water	Blood GSH levels, liver function, enzyme activity, behavioral changes	0.06[a]	Pletnikova, 1970

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[a] Calculated equivalent dose on dietary basis.

Obviously, if any of the effects discussed above prove to be actual toxic effects of selenium, the ratio of the toxic to beneficial dose of selenium would be decreased accordingly. However, the NAS Committee on Medical and Biologic Effects of Environmental Pollutants (MBEEP) concluded that the best indicator of chronic selenium poisoning is growth inhibition (NAS, 1976) and that 4 to 5 mg/kg dietary selenium are needed to demonstrate this effect in rats fed a normal diet. Clearly, more sensitive and specific criteria of selenium poisoning would be useful, and the development of such tests should be encouraged strongly.

Similarly, studies in people have been hampered by the lack of specific criteria for selenosis in humans. Smith _et al_. (1936) surveyed a rural population living in areas of the United States known to have a history of selenium poisoning in animals. They observed no symptoms that could be definitely related to selenium poisoning in humans and could link no serious illness to selenium poisoning. There were vague symptoms of ill health and symptoms suggestive of damage to the liver, kidneys, skin, and joints, but a causative role for selenium in these disorders could not be established. In a second survey, Smith and Westfall (1937) investigated the relationship between the incidence of these symptoms and the amount of selenium excreted in the urine. Although they considered none of the symptoms to be specific for selenium poisoning, increased incidence of gastrointestinal disturbances, icteroid discoloration of the skin, and bad teeth seemed to be associated with elevated urinary selenium levels.

Lemley (1940) examined a South Dakota rancher whom he considered to be the first described case of chronic selenium dermatitis in a human caused by the ingestion of selenium from natural sources. However, the patient's urinary excretion of selenium was normal, i.e., <0.100 mg/l (Glover, 1967). Moreover, administration of bromobenzene (C_6H_5Br), a compound known to increase urinary selenium output (Moxon et al., 1940), caused only a mild elevation in urinary selenium levels.

Lemley and Merryman (1941) described a South Dakota family whose members excreted 0.200 to 0.600 mg/l of selenium in the urine. One of these patients excreted 1.800 mg/l 24 hours after a course of bromobenzene. Dermatitis was not cited as one of the symptoms in this family. Rather, these cases were afflicted with various psychological disturbances such as clouding of the sensorium, extreme lassitude accompanied by depression, and moderate emotional instability. All members of the family also suffered from slight, continual dizziness, and they complained that their powers of concentration were markedly impaired.

Lemley and Merryman justified their diagnosis of selenium poisoning in these subjects on the basis of the following evidence: knowledge that the subjects lived in a seleniferous area; presence of concentrations of selenium in the urine above 0.100 mg/l; increased urinary elimination of selenium after administration of bromobenzene; and improvement of the subject's symptoms after elimination of selenium from the diet.

Jaffe (1976) found that the overall hemoglobin and hematocrit values of children living in a seleniferous area of Venezuela (Villa Bruzual) were lower than those of children living in Caracas, but there was no correlation between blood and urine selenium levels and hemoglobin or hematocrit values. Differences in hemoglobin were attributed to differences in nutritional or parasitological status and not to differences in selenium intake. Jaffe _et al_. (1972) showed that selenium poisoning decreased activities of prothrombin and serum alkaline phosphatase and transaminases in rats, but these activities were normal in all children studied. Dermatitis, hair loss, and abnormal nails were more frequent among the children in the seleniferous area than in those living in Caracas, but the cause of these clinical signs could not be determined definitively because of the lack of differences among the various biochemical tests performed.

The dose of selenium needed to cause chronic toxicity in humans is poorly defined. Smith and Westfall (1937) calculated that most of their subjects, who lived in highly seleniferous areas of the United States, were probably absorbing approximately 10 to 100 μg/kg body weight/day and that some of their subjects may have absorbed as much as 200 µg/kg/day. For a 70-kg human, these rates of absorption would be equivalent to an intake of 0.70 to 14.0 mg/day assuming that all of the selenium ingested was absorbed.

As discussed above, drinking water generally contributes little to the total daily selenium intake, but well water containing 9.0 mg/l caused hair loss, weakened nails, and listlessness in a family of Indians living in Colorado (Anonymous, 1962). Assuming a daily water consumption of 2 liters, this would represent a selenium intake of 18.0 mg/day. On the other hand, consumption of water containing 0.050 to 0.125 mg/l caused no increase in the incidence or prevalence of any of 85 health parameters measured in a population residing in a rural Colorado community (Tsongas and Ferguson, 1977).

Deliberate administration of selenium as selenite in oral doses of 50 µg/kg body weight/day for more than 1 year to patients with neuronal ceroid lipofuscinosis (NCL) caused no toxic manifestations (Westermarck, 1977). Rather, some of the NCL patients improved temporarily. A few of them exhibited a somewhat increased serum aspartate aminotransferase activity, but apparently this is not unusual in patients with NCL.

Schrauzer and White (1978) reported that consumption of 450 µg of selenium daily for 18 months in the form of a commercially available nutritional supplement along with 150 µg of selenium per day in the ordinary diet (total daily intake of 600 µg) produced no toxic effects in a well-fed individual although serum glutamic-oxaloacetic transaminase (SGOT) activities were somewhat elevated. Sakurai and Tsuchiya (1975) suggested a tentative maximum acceptable daily intake of 500 μg of selenium for the protection of human health. They obtained this value by multiplying a "low" mean normal daily selenium intake by humans (50 μg) by 10, a factor that appeared acceptable as a margin of safety within which the average human could tolerate selenium.

Interactions

In test animals, selenium has been shown to interact profoundly with several other elements. For example, selenium protects against the toxicity of several heavy metals including inorganic mercury (Parizek _et al._, 1971), methyl mercury (Ganther and Sunde, 1974), cadmium (Parizek _et al._, 1971), silver (Wagner _et al._, 1975), and thallium (Rusiecki and Brzezinski, 1966). Good correlations have been observed between the concentrations of mercury and selenium in the tissues of humans that have been exposed industrially to mercury (Kosta _et al._, 1975). The molecular mechanisms of the protective effects of selenium are not well understood. It is known that mercury may increase the nutritional requirement of animals for selenium (Froseth _et al._, 1974), while the toxicity of certain methylated selenium metabolites in rats is strongly potentiated by inorganic mercury (Parizek _et al._, 1971). Thus, mercury exposure is yet another situation in which the ratio of toxic to beneficial dose of selenium may be decreased.

Levander and Baumann (1966) reported that arsenic has a remarkable protective action against the toxicity of selenium in rats, apparently because it increases biliary excretion. However, arsenic has a strong synergistic toxicity with trimethylselenonium ion, one of the urinary excretion products of selenium (Obermeyer _et_ _al_., 1971).

In rats, dietary sulfate (SO_4^{2-}) has some protective activity against the toxicity of selenium ingested as selenate (SeO_4^{2-}), presumably by increasing urinary excretion (Ganther and Baumann, 1962).

Selenium has a strong inverse nutritional relationship with vitamin E in that the amount of selenium required to prevent deficiency diseases in chicks is increased as the dietary level of vitamin E decreases (Thompson and Scott, 1969). As shown in Table 16, selenium seems to exert a toxic effect at lower levels when animals are deficient in vitamin E. Therefore, vitamin E deficiency is another situation in which the ratio between the toxic and beneficial doses of selenium is decreased.

High levels of dietary protein afford some protection against selenium toxicity (Gortner, 1940). Linseed meal increases selenium residues in tissues but protects against selenosis (Halverson _et_ _al_., 1955; Levander _et_ _al_., 1970).

Bioavailability

Soluble inorganic salts of selenium are readily absorbed by animals, apparently without homeostatic control. Brown et al. (1972) reported that rats absorbed 95% or more of oral doses of selenite regardless of whether they were fed a selenium-deficient diet or a diet containing mildy toxic levels of selenium. Homeostatic control of selenium absorption in humans also appears to be lacking. Thomson (1974) observed that approximately 93% of milligram doses of sodium selenite (Na_2SeO_3) in solution was absorbed. However, only 60% of such doses was absorbed when the sodium selenite was given in the solid form, rather than in solution. This observation was puzzling in view of the high solubility of sodium selenite, and no explanation was offered.

The bioavailability of selenium in feeds was investigated by Cantor et al. (1975) who studied the ability of selenium in various poultry feedstuffs to prevent exudative diathesis, a selenium deficiency disease in chickens. In general, the selenium in plant products was more readily available than that in animal products. However, since the animal products consisted of highly processed fish and poultry meals, the availability of selenium in them may not resemble that in animal products consumed by humans.

Stewart _et_ _al_. (1978) reported that intestinal absorption of selenium was approximately 79% in New Zealanders who consumed foods providing 24 μg/day.

The Contribution of Drinking Water to Selenium Nutrition

The data in Table 13 indicate that most diets in North America provide approximately 0.150 mg of selenium per day. At this level of dietary intake, selenium in drinking water would contribute 0.1%, 1.3%, or 11.8% of the total selenium intake, depending on the concentration of selenium in the drinking water (Table 17). Thus, even when the selenium concentration in water is at the EPA limit of 0.01 mg/l, water would contribute only about 12% of the total selenium intake under conditions found in Canada and the United States. The relative contribution of drinking water to total selenium intake would be even lower in countries where foods contain high levels of selenium because of the high selenium concentrations in the soil, e.g., in Venezuela and certain areas in the United States. Drinking water might prove to be a valuable source of selenium in countries such as New Zealand where the soil concentrations and dietary intakes of selenium are quite low.

Research Recommendations

More sensitive and specific indicators of selenium toxicity are needed.

TABLE 17

Relative Contribution of Drinking Water to Total Selenium Intake at Different Concentrations of Selenium in Water and Different Dietary Intakes of Selenium[a]

Dietary Intake of Selenium, µg/day	Contribution of Water to Total Selenium Intake by Selenium Content of Water, %		
	0.1 µg/l	1.0 µg/l	10 µg/l
Low selenium diet, e.g., New Zealand			
24	0.8	7.7	45.5
Moderate selenium diet, e.g., North America			
150	0.1	1.3	11.8
High selenium diet, e.g., Venezuela			
326	0.06	0.61	5.8

[a] Assume water consumption of 2 l/day.

The physiological significance of biochemical changes caused by the ingestion of relatively low levels of selenium in the drinking water should be evaluated.

MANGANESE

Presence in Food, Water, and Air

Reviews of earlier data indicate that the average human dietary intake of manganese ranges from 2.0 to 8.8 mg/day (NAS, 1974; Underwood, 1977; WHO, 1973). More recently, Wolf (1979) has reported that the manganese intake of 22 subjects consuming self-selected diets (food and beverages) in the United States ranged between 1.1 and 6.4 mg/day (Figure 1) and averaged 2.8 mg/day. Guthrie and Robinson (1977) reported that the mean dietary manganese intake of 23 New Zealand women was 2.7 mg/day (range, 0.8 to 7.1 mg/day).

The Total Diet Study ("market basket" survey) conducted by the Food and Drug Administration (FDA) during fiscal year 1976 and 1977 indicated that typical American male teenagers and adults consuming a 3,900-Calorie diet ingested 3.8 and 3.7 mg of manganese per day respectively (FDA, 1978). In this survey, grains and cereal products were the richest dietary sources of manganese, contributing 57% to total manganese intake. Fruits and vegetables provided another 22%. Dairy products, meat, fish, and poultry made up only 4% of the total dietary manganese. Beverages, including drinking water, contributed 11% of the manganese intake, whereas oils, fats, shortening, sugar, and adjuncts contributed 6%.

The mean concentrations of manganese observed in various surveys of drinking water samples collected in different

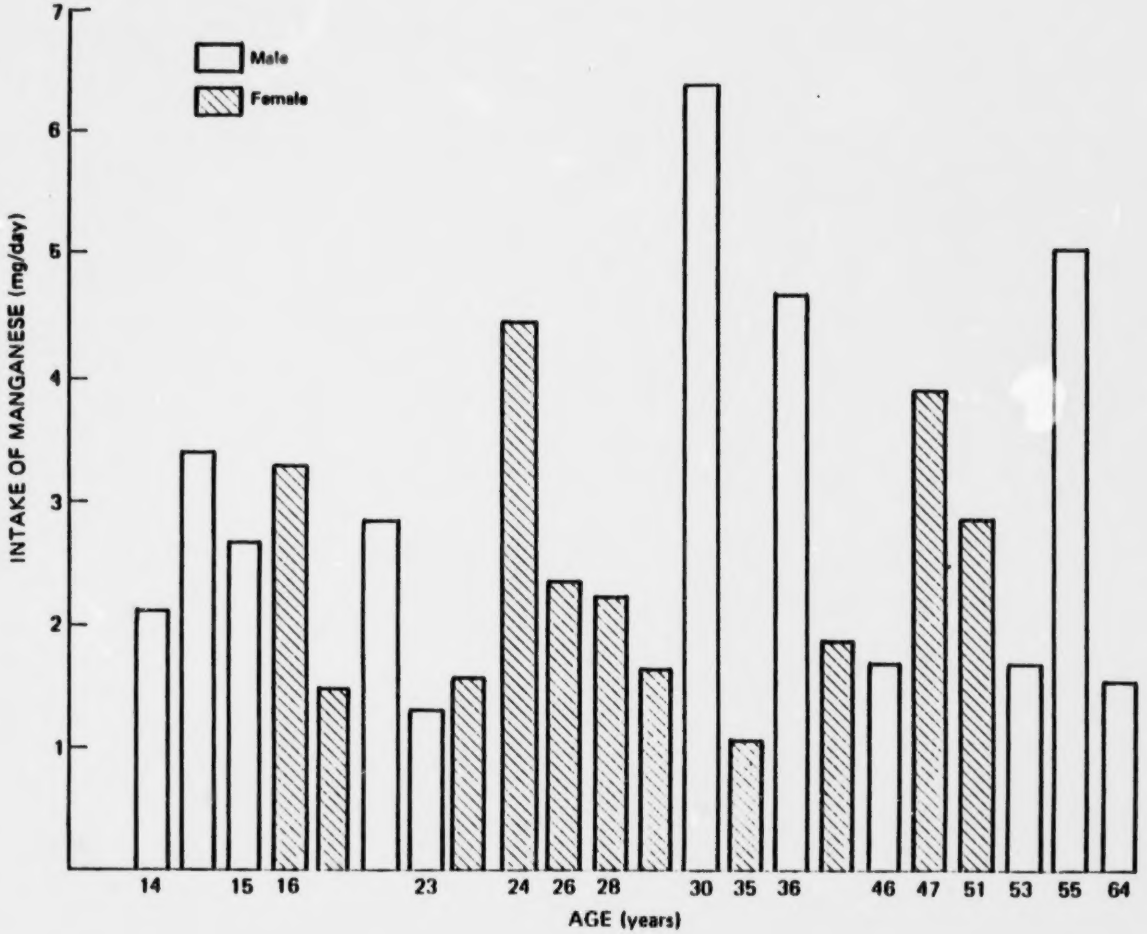

Figure 1 Average daily intake of manganese per subject per day as determined by analysis of self-selected diets. Data from Wolf, 1979.

parts of Europe and the United States are remarkably similar (Table 18). Although occasional high values were reported, 92% to 95% of the samples analyzed were below the drinking water standard of 0.05 mg/l (USEPA, 1975).

The concentration of manganese in ambient air is generally quite low. In 1968, the maximum average 24-hour manganese concentrations in three large cities in the United Staes were 0.09, 0.07, and 0.26 μg/m³ for Washington, Los Angeles, and Chicago, respectively (USEPA, 1975). Assuming that the general population is exposed to atmospheric concentrations of manganese of 0.1 μg/m³ and that a person ventilates 20 m³ of air daily, only 2 μg would be inhaled per day. This is less than 0.1% of the typical dietary intake of manganese.

Much higher concentrations of airborne manganese have been measured in cities with major manganese-emitting industries. For example, levels of 0.67, 1.10, and 14.0 μg/m³ were reported in East Chicago, Pittsburgh, and Johnstown, respectively (USEPA, 1975). In the Johnstown case, atmospheric manganese could contribute 280 μg to the daily intake, approximately 10% of that provided by the average American diet.

Distribution in Tissue

The concentration of manganese in various human tissues is shown in Table 19. Liver, pancreas, and kidney had the highest concentrations, and muscle the lowest. Schroeder *et*

TABLE 18

Concentration of Manganese in Drinking Water

Mean Manganese Concentrations, mg/1	Description of Sample	Comment	Reference
0.024 (range, <0.010-0.160)	Public water supplies from 19 European cities	18 samples contained <0.05 mg/1; one sample (from Odense, Denmark) contained 0.160 mg/1	Zoeteman and Brinkmann, 1977
0.022	969 public water systems located in nine geographic areas of the United States	8% of samples contained >0.05 mg/1; one sample contained 1.32 mg/1	Craun and McCabe, 1975; McCabe et al., 1970
0.032 ±0.013 (SE)	161 water supplies located in 44 states of the United States		Hadjimarkos, 1967
0.02 (range, <0.010-0.32)	902 samples of drinking water from the Boston, Massachusetts, area.	5% of the samples were >0.050 mg/1	Karalekas et al., 1976
0.026 (range, 0.0005-0.450)	380 drinking water samples obtained throughout the continental United States		Kopp, 1969
0.031 (range, 0.0026-0.152)	4,200 tap water samples obtained throughout the United States		Greathouse and Craun, 1979
0.017	Cold tap water samples from 50 households located in four municipalities in the Eastern United States		Strain et al., 1975

TABLE 19

Manganese Content of Certain Human Tissues[a]

Tissue	Manganese concentration, mg/kg, wet tissue
Liver	1.69
Pancreas	1.21
Kidney	0.97
Brain	0.34
Lung	0.26
Prostate	0.23
Heart	0.25
Spleen	0.15
Adrenals	0.18
Ovaries	0.18
Testes	0.15
Aorta	0.19
Muscle	0.07

[a] From Tipton and Cook, 1963.

al. (1966) estimated the total body pool of manganese in humans to be 20 mg.

Requirements

The NAS Committee on Animal Nutrition recommended a daily dietary intake of 50 mg of manganese per kilogram of diet to promote normal growth and gestation in rats (NAS, 1972). For poultry, the minimum dietary manganese requirement for normal growth, egg production, and hatchability is approximately 40 mg/kg of diet under normal dietary conditions; however, Underwood (1977) recommended a total intake of 50 mg/kg of diet to provide a margin of safety and to cope with variations in calcium and phosphorus intakes (see section on Interactions). A dietary manganese content of 50 mg/kg is sufficient to prevent perosis in chicks fed a diet based on ground corn and dried skim milk (Gallup and Norris, 1939).

Since no manganese deficiency has been recognized in humans, the usual manganese intake of 2 to 3 mg/day appears to be adequate for adults (WHO, 1973). The intake of manganese estimated by the Food and Nutrition Board of the National Research Council as adequate and safe is 2.5 to 5.0 mg for adults. It estimated correspondingly lower values for children and infants (NAS, in press) (see Table 31 included in the overall report Summary). Figure 1 indicates that a significant proportion of Americans are not consuming sufficient manganese in their food and beverages to meet the desirable level.

Toxicity versus Essential Levels

Dietary managanese levels as high as 1,000 mg/kg have no adverse effect on chicks (Gallup and Norris, 1939), but 4,800 mg/kg causes severe mortality in this species (Heller and Penquite, 1937). Levels of 500 mg/kg cause growth retardation and appetite depression in growing pigs (Grummer _et_ _al_., 1950), and only 45 or 125 mg/kg are needed to impair hemoglobin repletion in anemic lambs and pigs, respectively (Hartman _et_ _al_., 1955; Matrone _et_ _al_., 1959).

Neurobehavioral changes are probably the most subtle and sensitive effects of manganese toxicty. The neurological effects in nonhuman primates are similar to those in humans suffering from manganism. However, the NAS Committee on Medical and Biologic Effects of Environmental Pollutants (MBEEP) (NAS, 1973) concluded that "experimentally induced behavioral changes after manganese intoxication have scarcely been reported and dose-response relations are unknown..." Also, "experimental studies in animals, which appear to hold the key to full understanding of the pathophysiology of manganism, are extremely few and limited." Obviously more work along this line of investigation is needed.

Underwood (1977) stated that "manganese toxicity in man arising from excessive intakes in foods and beverages has never been reported and is difficult to visualize ever arising, except where industrial contamination occurs." Kawamura et al. (1941) reported an epidemic of manganese intoxication in Japan resulting from contaminated well water. They reported neurological symptoms and the deaths of two patients whose organs contained large quantities of manganese (and zinc, since the well water was also contaminated by this metal). Neither the total doses of manganese consumed nor the period of consumption were known, but samples of the well water contained approximately 14 mg of manganese tetroxide (Mn_3O_4) per liter. This would represent a dose of approximately 20 mg of manganese per day. The World Health Organization (WHO, 1973) found no evidence of manganese toxicity in individuals consuming 8 to 9 mg manganese/day in their food and has assumed that such levels are safe.

Underwood (1977) has pointed out that "manganese is among the least toxic of the trace elements to mammals and birds," but the ratio of the highly toxic dose (4,800 mg/kg) to the minimum dietary requirement for the growth of chicks (40 mg/kg) is only 120, not so different from that for selenium.

Interactions

The ability of manganese to interfere with the repletion of hemoglobin in anemic animals has been dicussed above. Hartman et al. (1955) suggested that the mechanism causing this effect may be a reduction by manganese of iron absorption. Others have shown that manganese inhibits the uptake of iron by perfused duodenal loops from iron-deficient rats (Thomson and Valberg, 1972). Increased manganese absorption is observed in iron-deficient animals (Diez-Ewald et al., 1968; Pollack et al., 1965) and humans (Mena et al., 1969). Thus, while high levels of manganese may cause anemia by interfering with iron absorption, iron deficiency may increase an individual's susceptibility to manganese poisoning (Mena et al., 1969).

Excess dietary calcium phosphate [$Ca_3(PO_4)_2$] increases the manganese requirement in chicks by reducing its bioavailability (Schaible and Bandemer, 1942).

Bioavailability

The gastrointestinal absorption of manganese is quite low, only 3% in healthy humans (Mena et al., 1969) and from 3% to 4% in rats (Greenberg et al., 1943). As discussed above, manganese absorption is increased by iron deficiency but decreased by excess dietary iron or calcium phosphate. Although early work suggested that the bioavailability of several inorganic salts of manganese was more or less equal for chickens (Gallup and Norris, 1939), more recent research, using chick leg abnormality scores, has demonstrated differences (Watson et al., 1971). Coupain et al. (1977) showed differences in the ability of various manganese chelates to promote normal reproduction rates and neonatal viability in rats.

Commenting on infant foods, Underwood (1977) said that "nothing is known of the form or availability of the manganese present in these foods, nor of how much is absorbed and retained." This is also true for the manganese in the foods and beverages of adult humans.

The Contribution of Drinking Water to Manganese Nutrition

Assuming a daily water intake of 2 liters, typical drinking water sources should contribute anywhere from 0.040 to 0.064 mg to the total daily intake of manganese. The higher amount would be less than 3% of that derived from the usual dietary sources. Some isolated water samples contained manganese levels as high as 1.32 mg/l which would contribute about as much as food to the total manganese intake.

Research Recommendations

More research should be conducted to establish dose/response relationships in experimentally induced behavioral changes and other toxic effects after manganese intoxication.

Further studies are needed to test the possible role of iron deficiency in potentiating manganese poisoning.

ARSENIC

Presence in Food, Water, and Air

For the past several years the U.S. Food and Drug Administration (FDA) has monitored arsenic and several heavy metals in its Total Diet ("market-basket") Survey program (Jelenik and Corneliussen, 1977). Each market-basket food composite represents the typical 2-week diet of a 15- to 20-year-old male in any one of four geographical regions of the United States.: South, Northeast, North Central, and West. The results of this survey for arsenic during the fiscal years 1967 through 1974 are shown in Table 20.

During 1971-1974, the average daily intake of arsenic was approximately 11.4 µg. About 82% of that amount was consumed in meat, fish, and poultry. No arsenic was detected in the beverage composite (including water) during these years. The difference between the values for 1967-1970 and those for 1971-1974 does not represent an actual drop in the dietary arsenic intake. Rather, it reflects an analytical artifact due to the development of a more sensitive and reliable method of arsenic analysis (Horwitz, personal communication). Estimates of the human dietary arsenic intake for earlier years were much higher (0.4 to 4.2 mg/day (Schroeder and Balassa, 1966; WHC, 1973) than the values reported by the FDA for 1971-1974. This suggested either that similar analytical problems were involved or

TABLE 20

Average Human Daily Intake of Arsenic from Dietary Sources[a]

	Average Intake by Fiscal Year of Sample Collection, μg/day							
Food Class	1967	1968	1969	1970	1971	1972	1973	1974
Vegetables, fruits, sugars oils, fats	9.1	23.6	7.6	2.3	1.5	ND[b]	ND	3.0
Grain and cereal products	3.0	22.1	8.4	ND	ND	ND	0.8	ND
Dairy products	9.9	6.1	3.8	4.6	ND	ND	1.5	ND
Meat, fish, and poultry	22.0	34.2	25.8	36.5	11.4	9.1	4.7	12.2
Beverages including water	7.6	18.2	11.4	ND	ND	ND	ND	ND
TOTALS	51.6	104.2	57.0	43.4	12.9	9.1	7.6[c]	16.0[c]

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[a] Recalculated from Jelenik and Corneliussen, 1977.

[b] ND = not detected.

[c] Total arsenic value is somewhat higher than sum of food class composites because traces of arsenic in certain vegetables and fruits were not given numerical values.

that there has been a drastic reduction in arsenic intake from dietary sources during recent years.

The lack of arsenic in the typical drinking water sampled by the FDA market-basket surveys has also been verified by surveys directed specifically at drinking water. McCabe et al. (1970) reported that only 0.4% of samples taken from various public water supplies in the United States exceeded the recommended limit for arsenic of 0.01 mg/l established by the U.S. Public Health Service (USPHS, 1962). Most other surveys have shown the average concentration of arsenic in drinking water to be only a few micrograms per liter (Table 21). One exception involved some deep wells in Indiana which produced water containing concentrations of arsenic up to 2.0 mg/l but by careful blending of this water with a source with a lower arsenic content it was possible for the supply management to bring the arsenic content of the total water supply within the mandatory (as opposed to recommended) limit of 0.05 mg/l (USPHS, 1962). Elevated levels of arsenic have also been found in the drinking water of Lane County, Oregon (Whanger et al., 1977), Antofagasta, Chile, (Borgono et al., 1977), the southwest coast of Taiwan (Tseng, 1977) and in certain European bottled mineral waters (Zoeteman and Brinkmann, 1977). Although five of the 13 types of bottled water analyzed contained less than 1 μg/l, the arsenic content of the eight others averaged 34 μg/l (range, 2 to 190 μg/l).

TABLE 21

Concentration of Arsenic in Drinking Water

Mean Arsenic Concentration and Range, µg/1	Description of Sample	Comment	Reference
0.9 (range, 0.5 to 1.6)	Public Water Supplies from six European cities		Zoeteman and Brinkmann, 1977
1.1 (range, 0.08 to 3)	Tap water from three Swedish cities		Boström and Wester, 1967
range, <1 to 50	Finished drinking water in midwestern United States	Single value of 50 µg/1 due to water from deep wells containing up to 2 mg/1	EPA, 1975
2.4 (range, 0.78 to 7.9)	4,200 tap water samples obtained throughout the United States	Represents two-thirds of all samples; one-third was less than detection limit of the analytical method used (0.78 µg/1)	Greathouse and Craun, 1978

The concentration of arsenic in air is generally quite low. In nonurban areas, the maximal average concentration was 20 ng/m³, but most values were less than 10 ng/m³ (NAS, 1977a). In New York City the average concentration of airborne arsenic was approximately 30 ng/m³. Assuming that 20 m³ of air is ventilated by humans daily, atmospheric arsenic in urban areas would contribute approximately 0.6 µg to the daily intake or about 5.3% of that derived from dietary sources. Of course, in certain regions, the concentration of arsenic in air may be much higher because of industrial or agricultural activities. For example, values as high as 2.5 mg/m³ have been reported in the vicinity of a smelter treating arsenical ores, and up to 141.0 mg/m³ was detected downwind from a west Texas cotton gin.

Distribution in Tissues

The concentrations of arsenic in certain human tissues are listed in Table 22. The liver had the highest concentration, and the heart the lowest. The total normal human body content of arsenic, which apparently tends to increase with age, has been given as 3 to 4 mg (NAS, 1977a).

Requirements

An increasing amount of evidence suggests that trace amounts of arsenic may play a beneficial nutritional role in

TABLE 22

Arsenic Content of Certain Human Tissues[a]

Tissue	Arsenic Concentration, mg/kg (wet tissue)
Liver	0.09-0.30
Lung	0.08-0.17
Kidney	0.07-0.14
Spleen	0.05-0.08
Thyroid	0.06-0.13
Pancreas	0.07
Intestine	0.07
Stomach	0.04
Heart	0.0001-0.016

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[a] Adapted from National Academy of Sciences, 1977.

animals. For example, Nielsen et al. (1975) reported that rats fed diets containing only 0.030 μg/g of arsenic had a roughness of their hair coat, low growth rate, anemia, splenomegaly, and increased erythrocyte osmotic fragility when compared to control rats that were supplemented with 4.5 μg/g arsenic. More recent work by Nielson and Shuler (1978a, b) has indicated that arsenic contributes to the maintenance of water and mineral balance in the chick and that the dietary requirement of the chick for arsenic is approximately 0.045 μg/g. Also, Anke and coworkers (1976, 1978) described the consequences of apparent arsenic deficiency in goats and minipigs fed semisynthetic rations containing less than 0.050 μg/g. The low-arsenic diet impaired reproduction and, in animals fed the diet for two generations, decreased weight gains. Schwarz (1977) reported that 0.5 to 2 μg/g of arsenic as sodium arsenite ($NaAsO_2$) stimulated the growth of rats fed diets containing less than 0.050 μg/g.

Toxicity versus Essential Levels

Experiments with laboratory animals have shown that several factors can influence the toxicity of arsenic (for a review, see NAS, 1977a). One of the most important of these factors is the chemical form of the arsenic itself. In general, soluble trivalent arsenic compounds are more toxic than pentavalent ones, and inorganic arsenicals also are more toxic than organic arsenicals. Elemental arsenic, being insoluble, is essentially nontoxic.

The physical state of the arsenic compound is also important since arsenic trioxide (As_2O_3) given orally in the solid form is much less toxic than the compound given in solution. Moreover, there are species-specific differences in susceptibility to arsenic poisoning. For example, Kerr et al. (1963) reported that 3-nitro-4-hydroxyphenylarsonic acid was much more toxic to turkeys and dogs than to chickens and rats.

A considerable body of literature provides qualitative descriptions of the signs and symptoms of arsenic poisoning in humans (reviewed in NAS 1977a, b), but few data concern quantitative dose-effect relationships. Vallee et al. (1960) estimated that the acute fatal dose of arsenic trioxide for humans is between 70 and 180 mg. This would be equivalent to a total arsenic dose of 53.2 to 136.8 mg, or, for a 70-kg human, 0.76 to 1.95 mg As/kg body weight. This is considerably less than the oral LD_{50} reported by Harrison et al. (1958) for arsenic as arsenic trioxide (As_2O_3) in the rat whether given in the solid form (145 mg As/kg body weight) or in solution (15.1 mg As/kg body weight). Thus, on a mg/kg body weight basis, humans appear to be much more susceptible than rats to the toxic effects of arsenic trioxide. The NAS Committee on Medical and Biologic Effects of Environmental Pollutants (MBEEP) pointed out that the rat may not be a suitable model for studying arsenic toxicity because of its peculiar metabolism of arsenic (NAS, 1977a). However, Harrison et al. (1958) reported that the oral LD_{50} for arsenic in Swiss mice was 39.4 mg/kg when administered as arsenic trioxide solution. Therefore, on a mg/kg body weight basis, rodents appear to be more resistant than humans to the toxic effects of arsenic. These results illustrate the caution that is needed when extrapolating arsenic toxicity data from rodents to humans.

Silver and Wainman (1952) described chronic human arsenic poisoning in their report of a patient who used Fowler's solution (which contains 10 g of arsenic trioxide per liter of solution) to treat asthma. This individual ingested approximately 6.69 mg of arsenic as arsenic trioxide daily for 9 months and then 3.35 mg daily for an additional 19 months. Increased freckling and darkening of nipples, indicative of arsenic poisoning, was first seen after 13 months along with intermittent bouts of nausea, cramps, and diarrhea. After approximately 1.5 years, the patient noted redness and puffiness about her eyes and patches of thickened skin (hyperkeratosis) on her palms and soles. Symmetrical, tender hepatomegaly was also observed. After 2.5 years, the patient became aware of neurological symptoms such as paresthesia and slight weakness of both hands. Once the arsenic was withdrawn, the pigmentation lightened, but the hyperkeratotic condition remained. Also, the asthma remained difficult to control. This history is useful because it allows a reasonably good estimate of the amount and duration of exposure necessary to produce toxic effects of arsenic in humans, whereas incidents of accidental arsenic poisoning generally do not permit this. However, many reports suggest that humans are highly variable in their degree and kind of response to arsenic exposure (NAS, 1977a).

Numerous epidemiological studies have suggested an association between chronic arsenic overexposure and certain diseases such as cardiovascular disease or cancer (reviewed in NAS 1977a, b). For example, people in Taiwan who consumed well water that contained 0.6 mg/l or more of arsenic had a 3 to 4 times higher rate of blackfoot disease (a peripheral vascular disorder resulting in gangrene of the extremities) than did people who consumed well water that contained 0.29 mg/l of arsenic or less (Tseng, 1977).

An increased incidence of bronchial and pulmonary diseases as well as cardiovascular pathology was observed in residents of Antofagasta, Chile, where the drinking water contained 0.8 mg/l of arsenic (Borgono and Greiber, 1972). These people also had increased abnormal skin pigmentation (Borgono et al., 1977) and increased cutaneous lesions such as leukoderma, melanoderma, hyperkeratosis, and squamous-cell carcinoma (Zaldivar, 1974). Moreover, Tseng (1977) observed an increased prevalence rate for skin cancer in the Taiwanese population that drank the arsenic-contaminated well water. Epidemiological studies have also indicated an association between occupational exposure to airborne arsenic and excess mortality due to lung cancer. Extrapolating from existent data, some investigators have suggested that a no-effect level, i.e., no increased risk of respiratory cancer mortality, might lie in the range of a few micrograms of arsenic per cubic meter of air (Blejer and Wagner, 1976).

The role of arsenic in carcinogenesis remains controversial. It has not been accepted universally as a carcinogen, largely because laboratory studies have not succeeded in producing tumors in animals (Fraumeni, 1975).

Although arsenic is generally considered to be highly toxic, it is actually much less toxic than selenium, a trace element with established nutritional value. For example, 31 mg/kg of dietary arsenic as sodium arsenite has no effect on the growth of rats (Byron _et_ _al_., 1967), whereas 5 mg/kg of dietary selenium as sodium selenite (Na_2SeO_3) is sufficient to cause growth retardation. If the nutritional requirement for arsenic as arsenite is 0.05 mg/kg of diet, then the ratio of the toxic to nutritional dose is approximately 1,250 since 62.5 mg/kg of arsenic as arsenite inhibited growth in rats (Byron _et_ _al_., 1967).

If 0.05 mg/kg of dietary arsenic is also a nutritionally desirable level for people, then the adequate human diet should provide a daily intake of approximately 25 to 50 μg. The current American diet does not meet this presumed requirement (Table 20). On the other hand, these levels of intake are not very far removed from those that have been associated with various human diseases (see above). Consequently the possible roles of arsenic in human health and disease urgently need to be clarified.

Interactions

The strong interaction between arsenic and selenium was discussed in the section on selenium. Administration of both arsenic and cadmium depressed weight gains in rats more than did either metal alone, but there did not seem to be any strong interactive effects of arsenic and lead (Mahaffey and Fowler, 1977).

Bioavailability

Water-soluble inorganic salts of arsenic are readily absorbed, but elemental arsenic and the insoluble arsenic sulfides are not. The unknown organic form of arsenic in shrimp and other shellfish is apparently absorbed well but is excreted rapidly in the urine (NAS, 1977a).

Contribution of Drinking Water to Arsenic Nutrition

As the nutritional requirement of arsenic for humans has not been proven, calculations on the contributions of drinking water to the arsenic requirement must necessarily be speculative. However, the extrapolation of animal data to humans (see above) gives a possible (calculated) need for 0.025-0.050 mg of arsenic daily. Two liters of water at an arsenic concentration of 0.0024 mg/l (which may be slightly higher than a typical value, see Table 21) would supply 10%-19% of this speculated need or 30% of the total intake of arsenic.

Conclusions

It is not possible to estimate the nutritional value of arsenic intake from water since the contributions calculated above are based on speculative values.

Research Recommendations

If the preliminary estimates of the need for arsenic in animals can be extrapolated to humans, the typical American diet may be marginally low in arsenic. Therefore, the possible beneficial nutritional effects of arsenic in animals and humans should be investigated further.

Additional research should be done in order to elucidate the relationship between levels of arsenic in the drinking water and the incidence of various human diseases, including cancer. A suitable animal model for the study of arsenic-induced cancer should be developed.

NICKEL

Presence in Food, Water, and Air

There is a wide variation in the nickel content of various foodstuffs. Thus, it is difficult to ascertain a definitive average daily dietary intake of nickel by humans. Various reported dietary intakes of nickel by huamns are listed in Table 23. The daily intake averages range from 165 to 500 µg.

In 1962, the nickel content of selected samples of public water supplies from the 100 largest cities in the United States ranged from 4 to 56 µg/l (Durfor and Becker, 1964). The samples were obtained of water at the source, in storage, and in various stages of treatment. Most of the samples contained less than 10 µg of nickel per liter. Only three samples contained more than 20 µg of nickel per liter. In 1969-1970, the average concentration of 969 U.S. water supplies (from 2,503 samples which were taken at the tap) was 4.8 µg/l (NAS, 1975). No nickel was detected in 21.7% of the samples, and only 25 of the 2,503 samples (1%) contained more than 20 µg/l. In another study, 3,676 tap water samples were collected in 35 different areas. Nickel was found in 83% of the samples in concentrations ranging from 0.4 to 5.1 µg/l (Greathouse and Craun, 1979).

The concentration of nickel in ambient air is generally quite low in nonurban areas. The Division of Atmospheric Surveillance of the National Air Sampling Network (NASN)

TABLE 23

Oral Intake of Nickel by Humans

Average intake, mg/day	Range, mg/day	Reference
NC[a]	0.300-0.600	Schroeder *et al.*, 1961
0.300	-	Taktakishvili, 1963
NC[a]	0.170-0.330	Tipton *et al.*, 1969
0.500	-	Louria *et al.*, 1972
NC[a]	0.280-0.310	Nodiya, 1972
0.451	0.288-0.696	Murthy *et al.*, 1973
0.165	0.107-0.221	Myron *et al.*, 1978

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[a] NC = Not calculated.

reported that nonurban air averaged 0.006 μg/m³ during 1965-1969 (NAS, 1975). McMullen et al. (1970) found that the ambient air of 30 nonurban stations scattered across the United States ranged from 0.002 to 0.008 μg/m³. Thus, if a person ventilates 20 m³ of air per day, only 0.04 to 0.16 μg of nickel would be inhaled daily in nonurban areas. The higher value is less than 0.1% of the dietary intake of nickel.

Urban air contains more nickel than does nonurban air. In urban areas, nickel is most concentrated near heavily traveled highways where it is probably derived from asphalt and automobile tires (Nielsen et al., 1977). The NASN Division of Atmospheric Surveillance reported that urban ambient air contained 0.017 μg/m³ in the spring and summer and 0.025 μg/m³ in winter (NAS, 1975). The average was 0.021 μg/m³. Cities with the highest air nickel level were Boston, East Chicago, Indiana, and Philadelphia, where the levels were near 0.100 μg/m³. McMullen et al. (1970) found that the ambient air from 217 urban stations contained 0.017 μg/m³. Assuming that urban air contains an average of 0.021 μg/m³ of nickel, an individual would inhale 0.42 μg of nickel daily, or less than 0.3% of the typical dietary intake. Even in cities with the highest concentration of nickel in ambient air, the inhalation of nickel would be less than 2% of the typical dietary intake.

Distribution in Tissue

Schroeder and Nason (1971) estimated that the human body contains 10 mg of nickel, or approximately 0.1 μg/g. They also suggested that 18% of the body nickel is found in the skin. Tissue analyses indicate that nickel is widely distributed in low concentrations (Table 24) and that bone and hair contain the highest concentrations.

Requirements

Because nickel is essential for animals (Nielsen, in press a), it is highly probable that it is also essential for humans. However, no nickel deficiency has been recognized in humans. Both Nielsen _et al_. (1975) and Schnegg and Kirchgessner (1978) suggested that the critical level of dietary nickel, below which deficiency symptoms are observed, is about 50 μg/kg of diet for chicks and rats. If animal data can be extrapolated to humans, then a 70-kg human consuming 1 kg of diet per day (dry basis) would have a daily requirement of 50 μg of nickel. The reported daily dietary intakes of 165-500 μg of nickel would adequately satisfy the presumed human nickel requirement.

Toxicity versus Essential Levels

The toxicity of nickel or nickel salts through oral intake is low, ranking with such elements as zinc, chromium, and manganese. Nickel salts exert their action mainly by

TABLE 24

Selected Examples of the Nickel Content of Human Tissues and Fluids

	Nickel Concent, µg/kg		
Tissue	Fresh	Dry	Reference
Bone	190-640	-	Nomoto, 1974
Hair	-	190-240	Nechay and Sunderman, 1973
Hair	-	1,010-4,050	Katz *et al*., 1975
Heart	6.0	23	Sunderman *et al*., 1971
Liver	9.0	32	Sunderman *et al*., 1971
Lung	16.0	86	Sunderman *et al*., 1971
	Nickel Content, µg/l		
Blood	23		Szadkowski *et al*., 1970
	4.8		Nomoto and Sunderman, 1970
	22		Delves *et al*., 1971
	6.0		Zachariasen *et al*., 1975
Saliva, parotid	1.9		Catalanatto *et al*., 1977

gastrointestinal irritation and not by inherent toxicity (Schroeder et al., 1961). The cause of this relative nontoxicity appears to be a mechanism in mammals that limits intestinal absorption of nickel.

Nickel also has little tendency to accumulate in tissues during lifetime exposure. Large oral doses of nickel salts are necessary to overcome the homeostatic control of nickel. Generally, 250 µg or more of nickel per gram of diet is required to produce signs of nickel toxicity in rats, mice, chicks, rabbits, and monkeys (Nielsen, 1977). Thus, the ratio of the minimum toxic dose and the minimum dietary requirement for chicks and rats is approximately 5,000. If animal data can be extrapolated to humans, this translates into a daily dose of 250 mg of soluble nickel to produce toxic symptoms in humans.

One isolated report indicates that lower levels of dietary nickel are toxic. Schroeder and Mitchener (1971) reported that 5 µg of nickel per milliliter of drinking water may be moderately toxic to rats during reproduction. After three generations of this exposure, the signs of toxicity included increased perinatal deaths and number of runts. The investigators reported that the size of the litters decreased with each generation and that few males were born in the third generation. These findings have not been confirmed.

Nickel dermatitis is a relatively common form of nickel toxicity. Several surveys indicated that the incidence of sensitivity to nickel is between 4% and 13% (NAS, 1975). Reviews (NAS, 1975; Nielsen, 1977) attributed nickel dermatitis to percutaneous absorption of nickel. However, Christensen and Moller (1975) suggested that the ingestion of small amounts of nickel may be of greater importance than external contacts in maintaining hand eczema. They observed that an oral dose of 5.6 mg of nickel as nickel sulfate ($NiSO_4$) produced a positive reaction in nickel-sensitive individuals within 1 to 20 hours after ingestion. That dose is only 11 to 34 times as high as the reported daily human dietary intake of nickel but 112 times as high as the human daily requirement of nickel that may be postulated from animal studies (50 µg/day; see above).

Interactions

Nickel interacts with at least 13 essential minerals in animals, plants, and microorganisms (Nielsen, in press b). Perhaps the most important interaction occurs with iron. Nielsen et al. (1978) reported that the interaction between dietary nickel and iron in rats affected hematocrit, hemoglobin level, plasma alkaline phosphatase activity, plasma phospholipid level, the ratio of liver weight to body weight, liver lipid extract yellow pigment, liver copper concentration, and, perhaps, liver manganese and nickel concentration. They also found that signs of nickel deprivation developed more rapidly and severely in rats when their diet contained borderline levels of iron. The data obtained from the borderline iron-deficient rats indicate that nickel deficiency impairs iron absorption. Schnegg and Kirchgessner (1976) suggested that the depressed levels of hemoglobin, erythrocytes, and hematocrit during nickel deficiency were caused by impaired iron absorption.

Bioavailability

Most ingested nickel remains unabsorbed by the gastrointestinal tract and is excreted in the feces. The limited data in Table 25 indicate that only 2%-3% of ingested nickel is absorbed. Nielsen _et_ _al_. (1978) suggested that elevated levels of dietary iron may enhance absorption of nickel.

The Contribution of Drinking Water to Nickel Nutrition

Assuming an estimated daily intake of 2 liters of water, these data indicate that typical drinking water sources would contribute anywhere from negligible amounts to 40 μg of nickel daily. The average contribution would probably be near 10 μg of nickel daily, which would be 2%-6% of that derived from usual dietary sources. However, isolated water samples assay as high as 75 μg of nickel per liter, and some individuals may be consuming diets that contain low amounts of nickel. Consequently, in some atypical instances, drinking water would contribute as much as or more than food to the total nickel intake.

TABLE 25

Percent of Ingested Nickel Found in Feces and Urine

Species	Ingested Nickel Found, %		Reference
	Feces	Urine	
Cow	96-98	-	O'Dell *et al*., 1971
Dog	90	10	Tedeschi and Sunderman, 1957
Human	-	3	Schroeder and Nason, 1971
Human	90	10	Nodiya, 1972
Rabbit	81	11	Babedzhanov, 1973
Rat	94-98	2-6	Elakhovskaya, 1972

Conclusions

Nickel deficiency in the typical U.S. diet is unlikely under present circumstances. Based on average food, water, and air concentrations, most drinking water contributes a very small proportion of the daily nickel intake. Only under unusual circumstances would nickel in drinking water contribute towards satisfying the presumed nutritional requirement of nickel or cause detrimental body burdens (i.e., help maintain hand eczema in nickel dermatitis).

VANADIUM

Presence in Food, Water, and Air

Recent studies have shown that the vanadium content of most foods is very low (Byrne and Kosta, 1978; Myron _et al_, 1977; Soremark, 1967; Welch and Cary, 1975), i.e., less than 1 ng/g. These studies differ from those of Schroeder _et al_. (1963) which are now generally assumed to be erroneous. Consequently, the 2 mg that Schroeder _et al_. (1963) estimated to be the daily average intake of vanadium is probably incorrect.

Only Myron _et al_. (1978) and Byrne and Kosta (1978) provide reasonable suggestions concerning the typical daily dietary intake by humans. Myron _et al_. (1978) ascertained the vanadium content of nine institutional diets and found that they would supply 12.4 to 30.1 µg of vanadium daily (average, 20 µg). Byrne and Kosta (1978) stated, "It can be estimated that the daily dietary intake is of the order of a few tens of micrograms, though it may vary over wide limits."

Vanadium occurs in water in several chemical forms of which the dioxyvanadium cation (VO_2^+) and the vanadate anion (VO_4^-) are readily soluble (Hopkins _et al_., 1977). However, the mobility of those ions in water is probably low because of easy adsorption on clay and precipitation with organic matter.

In 1962 the vanadium content of selected samples from the public water supplies of the 100 largest cities in the United States ranged from undetectable levels to 70 μg/l (median, <4.3 μg/l) (Durfor and Becker, 1964). The samples of water were obtained at the source, in storage, and in various stages of treatment. Water supplies from the Southwest generally contained higher vanadium concentrations than supplies from the Eastern states. Vanadium was detected in 26% of 3,676 tap water samples from 34 areas in the United States. The detected concentrations ranged from 1.3 to 33 μg/l (mean, 4.85 μg/l) (Greathouse and Craun, 1979).

Petroleum and other naturally occurring hydrocarbons such as asphaltite contain appreciable quantities of vanadium (Hopkins et al., 1977). Consequently, the combustion of petroleum products may contribute detectable amounts of vanadium to the atmosphere.

The amount of vanadium in ambient air is quite variable (ranging from undetectable to >2.0 μg/m³), depending upon location and season of the year (NAS, 1974). Urban atmospheres generally contain higher vanadium concentrations than air in nonurban areas. However, in 1965-1969 the National Air Sampling Network measured concentrations of vanadium in the rural areas of nine Eastern seaboard states from Maine to South Carolina that were significantly higher than those in other rural areas of the country (NAS, 1974). The concentrations in rural areas in the nine Eastern

Seaboard States were similar to those in urban air from the Midwestern and Western portions of the United States (2 to 64 ng/m^3).

Assuming that 20 m^3 is inhaled daily, ambient air would contribute 0.2% to 6% to the total daily intake of vanadium in some regions and cities in the United States. In some Eastern cities, ambient air would contribute as much or more vanadium as the typical diet. However, in regions other than the Eastern United States, ambient air would contribute probably less than 0.1% to the total daily intake of vanadium.

Distribution in Tissue

Byrne and Kosta (1978) estimated that the total body content of vanadium in healthy, adult humans is approximately 100 μg. Tissue analyses indicated that vanadium is widely distributed in very low concentrations in humans (Table 26). Hair and lung contain the most vanadium, probably as the result of exposure to atmospheric vanadium. The next highest concentrations occur in the bone, kidney, liver, teeth, and thyroid. The lowest concentrations are found in blood, brain, fat, and muscle tissue. The report of Byrne and Kosta (1978) showed that the estimate of Schroeder et al. (1963) (i.e., 17-43 mg of vanadium in the human body, of which 16 mg was in fat and 1.4 mg in serum) was most likely erroneous.

TABLE 26

Vanadium Content of Human Tissue and Fluids[a]

Tissue	Vanadium Content, ug/kg
Bile	0.65-1.85
Bone	0.8 -8.3
Blood	<0.5
Brain	<0.7 -0.75
Fat	0.3 -0.8
Heart	1.1
Hair	12 - 87 (average = 40)
Kidney	2.6-3.3
Liver	4.5-7.5
Lung	19 -140 (median 30)
Muscle	0.45-0.62
Teeth	<2.0-5.1
Thyroid	3.0-3.2

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[a] From Byrne and Kosta, 1978.

Requirements

Several reports suggest that vanadium is an essential element for chicks and rats (Nielsen, in press). However, the evidence for this is tenuous because of difficulties in obtaining a consistent set of signs that are indicative of vanadium deprivation. Apparently, the difficulty is related to the sensitivity of vanadium metabolism to changes in the composition of the diet (Nielsen, in press). It may be necessary to find a specific physiological role for vanadium in order to establish its essentiality.

The nutritional significance of vanadium is unclear because of the incomplete knowledge concerning the conditions that produce apparent vanadium deficiency and the dietary components that affect vanadium metabolism. As a result, it is difficult to suggest a vanadium requirement for any animal species, including humans. Estimates of the vanadium requirement of rats and chicks have ranged from 50 to 500 μg/kg of diet (Underwood, 1977). Those estimates are most likely too high. Under certain conditions, at least four independent laboratories have found that feeding less than 25 μg of vanadium per kilogram of diet adversely affected rats or chicks (Nielsen, in press). If animal data can be extrapolated to humans, then a 70-kg human consuming 1 kg of diet per day (dry basis) may have a daily requirement of approximately 25 μg of vanadium under certain dietary conditions. If that were true, the estimated daily dietary intake of vanadium (20 μg) would be borderline inadequate or adequate.

Toxicity versus Essential Levels

Diet composition also significantly alters the response of animals to elevated levels of dietary vanadium. For example, vanadium toxicity in chicks was alleviated by feeding corn, dehydrated grass, cottonseed meal, ascorbic acid, ethylenediaminetetraacetic acid (EDTA), and chromate (CrO_4^{2-}) (Berg, 1966; Berg and Lawrence, 1971; Hathcock et al., 1964; Hill, 1976). Nonetheless, under certain dietary conditions, 10 mg of vanadium per kilogram of diet was found to be slightly toxic to chickens, (Berg et al., 1963). That level of dietary vanadium is approximately 45 to 50 times the level at which apparent vanadium deficiency signs occurred in chicks. If animal data can be extrapolated to humans, a daily dose of 10 mg of vanadium may be slightly toxic in humans under certain conditions. That extrapolation is supported by Dimond et al. (1963) who gave oral doses of 4.5 to 18 mg vanadium per day to volunteers for 6 to 16 weeks. Cramps and diarrhea were produced only by the larger dose. Schroeder et al. (1963) fed up to 9 mg of vanadium per day for 6 to 16 months to older individuals who were confined to a mental institution. They observed no ill effects due to the vanadium supplementation.

Interactions

The apparent interaction of vanadium with various dietary components is discussed above in the sections on nutritional requirements and toxicity. The mechanisms by which various dietary components affect vanadium metabolism are not known. Furthermore, knowledge as to which specific dietary components affect vanadium metabolism is incomplete.

Bioavailability

Little is known about the availability of ingested vanadium. Apparently, most ingested vanadium remains unabsorbed by the gastrointestinal tract and is excreted in the feces. Curran et al. (1959) found that only 0.1% to 1.0% of a 100-mg dose of diammonium oxytartarcvanadate was absorbed from the human gut and that 60% of the absorbed vanadium was excreted by the kidneys within 24 hours. The remainder of the absorbed vanadium was retained by liver and bone.

The Contribution of Drinking Water to Vanadium Nutrition

Assuming a daily intake of 2 liters of water, data indicate that typical drinking water sources would contribute between negligible to 140 μg of vanadium daily. The average contribution is probably near 8 μg of vanadium daily which would be 40% of the amount of vanadium derived from usual dietary sources. In some instances, the contribution of drinking water to the daily intake of vanadium may be much greater than the contribution of the diet. For example, if the drinking water contained 33 μg of vanadium per liter, it would contribute three times as much vanadium as a typical diet.

Conclusions

Because the essentiality of vanadium has not been proven, no requirements have been established. However, it may have nutritional significance. For example, less than 25 μg of vanadium per kilogram of diet adversely affected rats and chicks under certain conditions. The typical diet in the United States probably supplies only 20 μg of vanadium daily, which may not provide an optimal intake of vanadium through the diet. Therefore, any contribution drinking water may give to the daily intake of vanadium may be beneficial.

SILICON

Presence in Food, Water, and Air

Since the essentiality of silicon as a trace element has only been established recently (Carlisle, 1969, 1970), little is known about its concentration in food. Older reports may be inaccurate because of contamination problems occurring during analysis. However, since food consumed by humans may also be contaminated, results obtained under clean laboratory conditions may also not be representative of human consumption. Generally, plants contain more silicon than do animal products. In plants, the proportions of silicon present as monosilicic acid (H_2SiO_3) and solid silica (SiO_2) vary with the species, stage of growth, and soil conditions (Bezeau _et al._, 1966). Substantial losses may occur during food processing, particularly in the refining of sugar (Hamilton and Minski, 1972/1973). Hamilton and Minski (1972/1973) determined that the mean total silicon intake from the diets of human adults in Great Britain was 1.2 ± 0.1 g/day.

The maximum, median, and minimum concentrations of silicon as silica in finished water from water supplies of the 100 largest cities of the United States were 72, 7.1, and zero mg/l (Durfor and Becker, 1964). No mean concentrations were given. Natural waters may contain from a few to several thousand milligrams of silicon per liter (Carlisle _et al._, 1977).

The information on concentrations of silicon in air is limited to special situations, e.g., the silicon in airborne asbestos particles.

Distribution in Tissues

Silicon enters the alimentary tract from the food as monosilicic acid, as solid silica, and in organic bound form with pectin mucopolysaccharides. Little is known about its absorption (Underwood, 1977).

Increased urinary silicon output with increasing intake up to fairly well-defined limits has been demonstrated in humans (Holt, 1950), rats (Keeler and Lovelace, 1959), and guinea pigs (Sauer et al., 1959). The rate of excretion does not seem to be dependent on the renal capabilities to excrete silicon but, rather, on the extent of silicon absorption. Body retention of silicon is small and occurs primarily in the bone.

Underwood (1977) reported that tissue levels of silicon vary greatly, that they are higher in humans than in the rat or the monkey, and that they decrease with age. The highest concentrations are found in human dental enamel (mean, 243 mg/kg). In the head and epiphysis of the femur of monkeys, silicon concentrations average 456 mg/kg. The silicon content of the normal human aorta decreases with age, and less silicon is present in arterial walls as arteriosclerosis develops. These are very interesting findings, but, because of the inherent difficulties encountered in analytical procedures, additional careful studies should be undertaken to substantiate them.

Requirements

The requirements for silicon in humans are unknown. Limited experiments with rats and chicks have shown that silicon is necessary for normal growth and satisfactory skeletal development (Carlisle, 1974). In rats, 50 mg/g of dry diet provided as water-soluble sodium metasilicate (Na_2SiO_3) fulfilled these requirements (Schwarz and Milne, 1972).

From studies of silicon-deficient and silicon-supplemented chickens, Carlisle (1974) concluded that silicon is involved in mucopolysaccharide and hexosamine synthesis. Thus, silicon effects the formation of cartilage and connective tissue. It also seems to hasten the rate of bone mineralization. Carlisle et al. (1977) reported that it reduced the water content of the bones of silicon-deficient chickens.

Toxicity versus Essential Levels

When inhaled into the lungs, particles of silica and asbestos may stimulate a severe fibrogenic reaction in the lungs and elsewhere in the body. Silica particles are phagocytized by alveolar macrophages where they interact with lysosomes (Nash et al., 1966). Furthermore, asbestos is now generally recognized as a carcinogen in humans. The potentials of silicate to induce pneumoconiosis and carcinoma are beyond the scope of this brief report. Further information on this subject can be found in Environmental Factors in Respiratory Disease (Lee, 1972) and in Occupational Lung Disorders (Parkes, 1974).

Ruminants consuming plants with a high silicon content may develop silicious renal calculi. Renal calculi in humans have been shown to contain silicates (Carlisle *et al*., 1977).

Grasses and sedges contain higher concentrations of silicon than do forbs and shrubs growing in the same locality (Bezeau *et al*., 1966). Thus, the proportional consumption of different plant material may determine whether ruminants would develop urolithiasis in specific areas.

The essentiality of silicon in chickens was established through carefully designed studies (Carlisle, 1972). Silicon deficiency was apparent when the diet contained 1 mg of silicon per kilogram of diet, while the presence of 100 mg of silicon in 1 kg of diet resulted in increased growth rate and increased water content of the long bones. Similarly, 50 mg of silicon per kilogram of diet prevented silicon deficiency in rats. It has not been established whether lower levels would have been equally effective.

Requirements for Nutrition

No information is presently available on essential dietary levels in humans.

Interactions

The interacton of silicon with molybdenum has been discussed by Carlisle (1979) but there is no well-substantiated information on the interaction of silicon with other trace elements. Ingestion of large amounts of silicon in the form of silica may interfere with the absorption of other nutrients.

Conclusions and Recommendations

Animal studies indicate that silicon is an essential trace element, but this has not been established in humans. There is no information on required daily intakes of humans.

Additional studies should be conducted to determine the availability of silicon in different forms and whether calcium and phosphates interact with silicon.

Since silicon can be found in appreciable amounts in mucopolysaccharide-rich tissues such as cartilage, it should be determined how silicon affects the development and maintenance of cartilage and calcification of bone. It should also be established whether silicon plays any role in the healing of fractures. Further careful studies should be conducted to determine levels of silicon in food and human tissues.

MOLYBDENUM

Presence in Food, Water, and Air

Molybdenum occurs in nature with valences of 4+, 6+, and, possibly, 3+ and 5+. It is contained in minerals such as molybdenite (MoS_2), wulfenite ($PbMo_4$), ferrimolybdate ($FeMoO_3 \cdot H_2O$), and jordisite (amorphous MoS_2).

The widely varying environmental concentrations of molybdenum are caused by regional geological factors. Concentrations in water and soil may vary by a factor of more than 10 causing both deficient and excessive intake of molybdenum for plants and ruminants, depending on their location. In areas where molybdenum ore is processed, concentrations in soil and water may increase considerably. In soil, the available molybdenum is of greater importance for plant nutrition than is the total amount of molybdenum. The availability is dependent on pH (i.e., it is greater in alkaline soils) and other factors in the soil.

The amount of molybdenum in vegetable crops is greatly influenced by the molybdenum content of soil. Engel _et_ _al_. (1967) determined that the molybdenum in the dry matter of the diet ranged from 94-189 µg/kg. Jacobson and Webster (1977) stated that ordinary hospital diets provided from 44 to 1,000 µg of molybdenum per day. Schroeder _et_ _al_. (1970) determined molybdenum concentrations in a variety of foods on a wet-weight basis. The concentrations ranged from none to 21.40 mg/kg in beef kidney. Molybdenum was associated with most foods that contained purine. Table 27 shows some representative food contents of molybdenum. The richest sources were meats, grains, and legumes; the poorest were vegetables other than legumes, fruits, sugar, oils, and fats. However, Friberg et al. (1975) concluded that diets based on leafy vegetables and legumes would result in a higher intake of molybdenum than those based mainly on meat products.

In balance studies with healthy children, Alexander et al. (1974) determined that a total molybdenum intake of 3.02 μg/kg body weight resulted in the absorption of 2.32 μg of molybdenum per kilogram of body weight. Of this, 42% was retained and 1.76 μg/kg was excreted.

Schroeder et al. (1970) estimated that the average diet in the United States contained 335 μg of molybdenum (range, 210-460 μg). In the USSR, estimates of intake by children were 156-161 μg/day (Vorob'eva and Osmolovskaya, 1970) and in adults, 329-376 μg/day (Gabovich and Kulsyaya, 1964). Hamilton and Minski (1972/1973) studied total diets from different regions of the United Kingdom. They reported an average daily intake of 128 μg of molybdenum (SD ±34).

Kopp and Kroner (1967) measured trace metals in rivers and lakes of the United States from 1962-1967. They detected molybdenum in 32.7% of 1,577 samples (range, 2-1,500 μg/l; mean, 68 μg/l). Durfor and Becker (1964) reported that the median concentration of molybdenum in finished water in public water supplies was 1-4 μg/l and

TABLE 27

Molybdenum Concentration in Food[a]

Food Item	Molybdenum Concentration, μg/g wet tissue
Seafood	0 - 0.56
Ground beef	0
Beef Liver	1.97
Beef Kidney	21.40
Pork loin	3.68
Lamb chops	5.00
Milk products	0 - 0.49
Grains and cereals	0.46 - 5.87
Vegetables:	
legumes	0 - 4.8
roots	0 - 0.59
vines	0 - 0.34
leafy	0 - 0.11
Fruits	0.3 - 0.79

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[a] Data from Schroeder *et al*., 1970

that the maximum concentration was 68 μg/l. Greathouse and Craun (1979) detected molybdenum in 30% of 3,676 tap water samples. The maximum concentration was 52.7 μg/l, the mean concentration was 8.05 μg/l, and the minimum concentration was 1.1 μg/l.

Air quality data from the National Air Sampling Network indicated that molybdenum concentrations in ambient air in the United States during 1966 ranged from 10 to 30 ng/m³ in urban areas and from 0.1 to 3.2 ng/m³ in nonurban areas (USPHS, 1968). Fly ash from power stations may contain as much as 10-40 mg/kg (Smith, 1958).

Distribution in Tissues

The hexavalent compounds, molybdenum trioxide (MoO_3) and calcium molybdate ($CaMoO_4$), are absorbed quite well from the gastrointestinal tract but, apparently, molybdenum sulfide and molybdnite are not (Gray and Daniel, 1954). The absorption of molybdenum given orally as molybdenum trioxide to guinea pigs was 85% (Fairhall et al., 1945). Similarly, Van Campen and Mitchell (1965) showed ready absorption of ammonium molybdate [$(NH_4)_2{}^{99}MoO_4$] from the gastrointestinal tract of rats. In humans, between 25% and 80% of ingested molybdenum is absorbed (Alexander et al., 1974; Bostrom and Wester, 1968; Robinson et al., 1973; Tipton et al., 1969).

Hexavalent molybdenum is rapidly excreted by animals over a 2-week period (Amon et al., 1967). In humans, 30%-40% of an intravenous dose was excreted within 10 days

(Rosoff and Spencer, 1964). The highest concentrations of molybdenum in tissue were found in kidney, liver, and bone (Anke *et al.*, 1971; Durbin *et al.*, 1957).

Normal blood values in humans vary a great deal but are usually in the ng/ml whole-blood range. Molybdenum levels seem to increase in the kidneys and liver in the second and third decade of life. On the average, the liver reaches a concentration of 0.5 to 1 µg/g and the kidneys, 0.25 µg/g on a wet-weight basis (Friberg *et al.*, 1975). Molybdenum concentrations in tissues from 150 victims of accidental deaths in the U.S. are listed in Table 28. When tissues were analyzed on a wet-weight basis, molybdenum was usually not found in other organs. However, on an ash basis µg/g concentrations of molybdenum were found in a number of other organs.

Venugotal and Luckey (1978) reported that 9.3 mg was the average content of molybdenum in the human adult body.

Requirements

Minimum dietary requirements for molybdenum in animals and humans are presently unknown. Requirements for molybdenum in rats and chickens are very low (Higgins *et al.*, 1956). Attempts at inducing molybdenum deficiency have been successful only when tungstate ($WO_4^=$) an inhibitory metal, was given concomitantly (Friberg *et al.*, 1975). Recently, Anke *et al.* (1977) have been able to induce molybdenum deficiency in goats by feeding them a diet

TABLE 28

Molybdenum in Human Tissues[a]

Organ	Molybdenum Concentration, μg/g wet tissue
Adipose tissue	0.0055
Blood	0.041
Liver	1.1
Lungs	0.016
Heart	0.017
Kidneys	0.37

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[a] Data from Schroeder *et al*., 1970

containing less than 60 μg of molybdenum per kilogram of diet. Similar molybdenum deficiencies in poultry have been described by Payne (1977).

The daily intake of molybdenum from dry diet in adults has been estimated as 0.1 mg/day, or approximately 0.13 mg/kg of diet. Several balance studies in humans (Engel et al., 1967; Tipton et al., 1966) suggested that a slightly positive balance is maintained if the diet provides approximately 2 μg of molybdenum per kilogram of body weight per day. An estimated adequate and safe intake of molybdenum for humans of 0.15-0.5 mg/day has been established (NAS, in press; see Table 31 in the report summary). The essentiality of molybdenum is based on the fact that it is an integral part of many enzymes.

The flavoprotein enzyme xanthine oxydase is a molybdenum-containing metalloenzyme. Aldehyde oxidase and sulfite oxidase are also dependent for their activity on the presence of molybdenum (Cohen et al., 1971; Higgins et al., 1956; DeRenzo et al., 1953; Richert and Westerfeld, 1953).

The beneficial effect of molybdenum on the incidence and severity of dental caries has been refuted by Hadjimarkos (1968). He pointed out that the lower prevalence of caries in children from the high molybdenum area in the earlier studies could have resulted from the presence of fluoride since teeth from the children of this group were reported to contain 34% more fluoride than the teeth of the children from the low molybdenum area (Hadjimarkos, 1973).

Toxicity versus Essential Levels

In rats and rabbits, dietary levels ranging from 500 to 5,000 mg/kg diet produce weight loss and, in most instances, anemia (Arrington and Davis, 1953; Gray and Daniel, 1954; McCarter *et al.*, 1962). Bone deformities were also noted (Arrington and Davis, 1953; McCarter *et al.*, 1962; Vallie *et al.*, 1969; Lalich *et al.*, 1965).

Among livestock, cattle seem to be more sensitive to the toxic effects of molybdenum than are sheep, horses, and pigs. Severe molybdenosis in cattle occurs under natural grazing conditions in many parts of the world (Britton and Goss, 1946; Cunningham, 1957; Dye and O'Hara, 1959; Ferguson *et al.*, 1938).

Both occupational and high-level dietary exposure to molybdenum have been linked to elevated uric acid levels in blood and an increased incidence of gout.

Akopajan (1964a) examined 73 workers in a copper-molybdenum plant and 10 control subjects. He observed the highest levels of uric acid in the blood of miners who had been exposed to the highest concentrations and who complained of arthralgia. However, his results are difficult to evaluate since he did not report the blood levels of uric acid or the concentrations to which the subjects were exposed. In a later report, Avakajan (1966) described hyperuricemia in 85 workers in a copper-molybdenum plant in Kadzaran.

Kovalskii et al. (1961) and Yarovaya (1964) reported a high incidence of gout in an area of Armenia where the concentrations of molybdenum and copper in the soil were 77 mg/kg and 39 mg/kg, respectively. In 1961, using molybdenum and copper levels in different food products as a basis, the investigators calculated the total daily intakes for an adult man in this area to be 10-15 mg molybdenum and 5-10 mg copper compared to the intake of a man in a control area which was 1-2 mg molybdenum and 10-15 mg copper.

A survey of 262 18-year-old and older subjects from two villages in the molybdenum-rich area revealed a prevalence of symptoms similar to gout in 31% of the subjects from one village and 18% from the other. The authors claimed that similar symptoms normally occurred in 1%-4% of the population of the USSR. The symptoms were characterized as arthralgia in the knees, hands, and feet. Deformities of the joints were also reported.

In some areas of India, where sorghum apparently contains high concentrations of molybdenum, a bone-crippling disease has been observed among the population. A definite cause-effect relationship has not been established, but it is possible that molybdenum increases the toxicity of fluoride (FDA, 1975).

Depending on the amount of copper, fluorides, and other nutrients in the diet and the solubility of the molybdenum salt, a concentration of 10-15 mg of molybdenum in the diet may result in chronic toxicity in humans (Underwood, 1977).

This concentration is at least 20 times higher than the upper limit of the provisional recommended dietary allowance presently under consideration.

Interactions

Copper compounds have had a beneficial effect on molybdenosis (Cook et al., 1966; Cunningham, 1957). In New Zealand, Cunningham (1950) found that the onset of scouring (molybdenosis) was delayed until copper stores in the tissue were depleted (Cunningham, 1950). Based on experimental evidence, Miltmore and Mason (1971) claimed that the critical ratio of copper to molybdenum is 2.0 to prevent molybdenosis; however, Alloway (1973) believes that it is closer to 4.0. Since the levels in New Zealand are generally lower than those in England, ratios may vary with different molybdenum concentration.

Experimental studies further elucidate this interaction between molybdenum and copper, which is modified by other dietary factors such as the amount of sulfate, manganese, and protein in the diet. Gray and Daniel (1954) showed that small amounts of molybdenum could produce toxicity in rats on copper-deficient diets. This effect was intensified by the simultaneous addition of sulfate (SO_4). In rats with adequate dietary intake of copper, large amounts of molybdenum were necessary to produce the same effect while molybdenosis could be completely prevented by the addition of sulfate to the diet. Studies primarily in sheep seem to indicate that sulfates in the diet may have either adverse or beneficial effects depending upon the copper status. Dick (1956) found that daily doses of 0.3 to 100 mg molybdenum in sheep on a low dietary intake of sulfate had no effect on blood copper levels, but when sulfate intakes were high, blood copper levels rose rapidly in response to 60- or 90-mg doses of molybdenum. Sulfates also increase the urinary excretion of molybdenum (Dick, 1953) in sheep but at high concentrations decreased the molybdenum excretion in milk (Hogan and Hutchinson, 1965).

Sulfides also seem to affect the metabolism of molybdenum and copper. A number of investigators have attempted to explain the complex interaction between copper, molybdenum, and sulfide. Apparently, exposure to molybdenum decreases the activity of sulfide oxidase in the liver (Mills et al., 1958). Excessive dietary intake of cystine by rats given high concentrations of molybdenum increased molybdenum toxicity (Halverson et al., 1960). An accumulation of sulfide in the tissues as a consequence of depressed sulfide oxidase activity occurs in molybdenotic rats (Van Reen, 1954; Williams and Van Reen, 1956). In the digestive tract, copper interacts with molybdenum and copper availability may be depressed through the precipitation of insoluble cupric sulfide (Cu_2S_3) (Mills, 1961). Furthermore, cupric molybdate [$Cu_2(MoO_4)_3$], a biologically unavailable compound, may form in the digestive tract, and if sulfate at relatively neutral pH is reduced to sulfide, thiomolybdate may form. This molybdate may complex with copper (Huisingh et al., 1973; Suttle, 1975). Much of the research on the interaction of molybdenum with copper in the digestive tract was done in sheep. It is presently not known whether similar interactions would occur in humans.

Interactions between molybdenum, iron, and fluorides are not well understood.

Contribution of Drinking Water to Molybdenum Nutrition

Assuming that the estimated dietary intake of molybdenum from dry diet is 100 µg/day in areas where the concentration in water is high, the amount contributed by drinking water may be substantial. For a daily consumption of 2 liters of water this contribution could range from approximately 2 to 136 µg, according to Durfor and Becker (1964). However, high concentrations in public water supplies seem to be infrequent. Durfor and Becker reported the median concentration of molybdenum in finished water to be 1-4 µg/l. This amount could result in a daily intake of 2 to 8 µg molybdenum, which would constitute only 1.3 to 5.3% of the lower limit of the estimated adequate and safe intake NAS, in press).

Conclusions and Recommendations

Evidence seems to indicate that molybdenum is an essential trace element. Since it is only required in very low concentrations, it has been difficult to produce deficiency diseases in animals. Further studies should be conducted in this area under well-controlled conditions.

Our understanding of chronic molybdenum toxicity or deficiency in humans is presently extremely limited. This topic should be studied. Futher studies should also be conducted to determine the interaction of molybdenum with other elements and nutrients in humans.

Factors affecting absorption and availability of molybdenum in humans should also be determined. The reduction of molybdenum in water in areas with high molybdenum concentrations should not be attempted until it has been determined whether molybdenum is absorbed in the form in which it occurs in water. The effect of such a reduction on other nutrients such as copper and fluoride should be determined.

CHROMIUM

Presence in Food, Water, and Air

Although some of the difficulties in analyzing biological material for chromium have been overcome during the past few years, the methods are still not satisfactory (Mertz, 1976; Mertz et al., 1978). Because of these analytical difficulties, the accuracy of many of the chromium values in the literature is suspect.

The nutritional value of chromium in foods is complicated by the fact that it is not all present in the most biologically active form, i.e., as glucose tolerance factor (GTF) (Mertz, 1976). The bioavailability of inorganic chromium in foods is very low. Trivalent chromium is the nutritionally useful form; hexavalent chromium is not. Thus, total chromium content may not be a valid indicator of the contribution a food will make towards meeting the chromium requirement. Although a reproducible method for assaying biologically active chromium has been developed (Brantner and Anderson, 1978), a direct and accurate quantitative analysis of GTF in tissues and foods has not. Most likely, when a routine quantitative analysis for GTF is developed, the nutritional value of chromium will be expressed in that manner, just as the nutritional value of cobalt in foods is expressed as vitamin B_{12} activity. Because there is no better measure, total chromium content is still used.

Perhaps the most accurate determination of the mean daily chromium intake in the United States was made by Kumpulainen _et_ _al_. (in press). They found that 14 "typical self-selected American diets"--typical with regard to fat and calories--supplied 37 to 130 μg of chromium daily (average, 62 μg). The mean daily intake was similar to that found earlier for subjects consuming institutional diets and for young people on a free choice diet (Levine _et_ _al_., 1968; Schroeder _et_ _al_., 1962).

The limited data on the chromium content of drinking water in the United States are summarized in Table 29.

The chromium concentration in air varies with location. Towill _et_ _al_. (1978) cited data from the U.S. Environmental Protection Agency which showed that the chromium concentrations in most nonurban areas were below detection levels. In urban areas, the yearly average concentrations varied from below detection levels to as high as 0.120 μg/m^3. Yearly averages were greater than 0.01 μg/m^3 in only 59 of 186 urban areas. Those values were similar to the values compiled by the National Air Sampling Network (cited by Towill _et_ _al_., 1978), which showed the national average for chromium in air to be 0.015 μg/m^3 and a maximum of 0.350 μg/m^3. Thus, if a person ventilates 20 m^3 of air/day, ambient air in most areas of the United States would contribute less than 0.5% to the daily intake of chromium. Even in cities with the highest concentration of chromium in

TABLE 29

Studies on Chromium in Drinking Water in United States[a]

Number of Samples	Chromium concentration, μg/l Minimum	 Maximum	 Mean
100[b]	ND[c]	35	0.43 (median)
2,595	NR[d]	79	NR[d]
1,577	1	112	9.7
380	1	29	7.5

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[a] Data from Durfor and Becker, 1962; Kopp, 1969; and U. S. Department of Health, Education, and Welfare, 1970.

[b] Samples from public water supplies of 100 largest cities in the United States.

[c] ND = not detected.

[d] NR = not reported.

ambient air, the inhalation of chromium would probably be less than 4% of the typical dietary intake.

Distribution in Tissues

Because the analytical methods are inadequate, most of the reported values for the chromium content of tissue are probably inaccurate. It is generally accepted that the concentrations of chromium are very low. This is supported by Doisy *et al*. (1976), who reported 1 to 5 ng of chromium/ml in plasma, and by Guthrie *et al*. (1978), who found less than 1 ng of chromium per milliliter of urine.

Requirements

Data on older subjects, diabetics, pregnant women, and malnourished children suggest that chromium deficiency does occur in humans (Doisy *et al*., 1976; Gurson, 1977). Jeejeebhoy *et al*. (1977) described a case of chromium deficiency in a woman who was maintained on total parenteral nutrition for several years. Their findings suggested that the signs of chromium deprivation in humans include glucose intolerance, inability to utilize glucose for energy, neuropathy with normal insulin levels, high free fatty acid levels, a low respiratory quotient, and abnormal metabolism of nitrogen. Although it is apparent that chromium is an essential nutrient, the estimation of the dietary chromium requirement is difficult because of the great difference in bioavailability of this element in different foods. Nonetheless, an estimated adequate and safe intake for chromium of 50-200 μg/day has been established (NAS, in press). The lower value of 50 μg was based on the average chromium intake in the United States from mixed diets and the lack of evidence of widespread, serious chromium deficiency related to this intake. Thus, the 62 mg average daily dietary intake of chromium, which was estimated by Kumpulainen _et al_. (in press) would be just adequate to meet the minimal value.

Toxicity versus Essential Levels

The toxicity of chromium depends upon its valence. Trivalent chromium, which is the nutritionally active form, has such a low order of toxicity that a wide margin of safety exists between amounts ordinarily ingested and those which induce deleterious effects. The National Academy of Sciences committee on chromium stated: "Compounds of chromium in the trivalent state have no established toxicity. When taken by mouth, they do not give rise to local or systemic effects and are poorly absorbed. No specific effects are known to result from inhalation. In contact with the skin, they combine with proteins in the superficial layers, but do not cause ulceration" (NAS, 1974).

Hexavalent chromium is much more toxic than trivalent chromium, but has no nutritional value. Hexavalent chromium may be absorbed by ingestion, through the skin, and by inhalation. Generally, hexavalent chromium compounds cause irritation and corrosion. Signs of toxicity by these compounds include hemorrhage of the gastrointestinal tract after ingestion, ulceration of the nasal septum and cancer of the respiratory tract from inhalation, and cutaneous injury (ulceration and both eczematous and noneczematous contact dermatitis) upon dermal exposure (NAS, 1974).

Trivalent chromium also provokes allergic skin responses in chromium-sensitive subjects. However, a greater concentration of trivalent test material is needed than for hexavalent chromium because the trivalent forms are less soluble and less absorbable. Hexavalent chromium is reduced within the skin to the trivalent state. Methionine, cystine, and cysteine can bring about this reduction (Samitz and Katz, 1963). The National Academy of Sciences committee on Medical and Biologic Effects of Environmental Pollutants (MBEEP) suggested that the trivalent form resulting from the reduction may form haptene-protein complexes thereby initiating sensitization (NAS, 1974).

Hexavalent concentrations of 50 μg chromium per gram of diet have been associated with growth depression and liver and kidney damage in laboratory animals (Mackenzie _et al._, 1958). Symptoms of excessive dietary intake of chromium in humans are unknown. Thus, if the most toxic form of chromium (hexavalent) is used and if the minimum toxic dose is assumed to be near 50 μg/g of diet, the ratio of the minimum toxic dose and the minimum RDA for humans is aproximately 1,000. This ratio would be much higher if the minimum toxic dose of trivalent chromium were known.

Interactions

Perhaps the best known interaction between chromium and another trace element is that with vanadium. Wright (1968) found that high dietary chromium (500-2,000 μg/g) was effective in overcoming growth depression and mortality in rats that had been fed 20 mg of vanadate per kilogram of diet. On the other hand, Hunt and Nielsen (1979) reported that 500 μg of chromium (as the acetate) per gram of diet caused relatively small amounts of vanadium (5 μg/g of diet) to be toxic for the chick.

Bioavailability

The mechanisms through which chromium is absorbed from the gastrointestinal tract are poorly understood. It is known that the bioavailability of chromium is dependent upon its chemical form. Biologically active chromium (i.e., as the GTF) is quite available. For example, the absorption in the rat of chromium extracted from Brewer's yeast (a good source of GTF) ranged from 10% to 25% of the given dose (Mertz, 1976). On the other hand, the absorption of trivalent inorganic chromium is presumed to be 1% or less (Doisy et al., 1976). However, Polansky and Anderson (1978) reported that rats absorbed from 5% to 10% of radioactive trivalent chromium (as the chloride) within 5 minutes after it was administered by stomach intubation. The chromium retained by the rats decreased from 5% to 10% at 5 minutes to less than 1% at 1 hour. Apparently, most of the quickly absorbed chromium was lost via the gastrointestinal tract. Their data indicated that the absorption of trivalent chromium is approximately 10-fold higher than previously presumed, that it occurs within minutes of administration, and that it is retained for less than 1 hour. Contrary to current thinking, their data suggest that urine may not be the most important excretory pathway for all absorbed chromium.

Contribution of Water to Chromium Nutrition

Table 29 shows that typical drinking water sources would contribute anywhere from negligible amounts to 224 μg of chromium daily if 2 liters of water were consumed. The average contribution would probably be near 17 μg of chromium daily, which would be approximately 27% of that derived from the usual food sources or 22% of the total intake from food and liquids. In some instances, the contribution of drinking water to the daily intake of chromium may be greater than the contribution of the diet. For example, if the drinking water contained 50 μg of chromium per liter (the Environmental Protection Agency Maximum Contaminant Level for drinking water; USEPA, 1975), it would contribute almost twice as much chromium as does food in a typical diet.

Conclusions and Recommendations

Chromium is an essential nutrient for humans. Based on average concentrations in food, water, and air, drinking water could contribute a substantial proportion of the daily chromium intake. Unfortunately, drinking water probably contains the inorganic form of chromium. This form has poor bioavailability and retention. Nonetheless, any amount that drinking water contributes to the daily intake of chromium may be beneficial because chromium intake via the diet may not always meet the provisional RDA set for humans. Moreover, evidence suggests that chromium deficiency may be a problem in the United States.

The subcommittee recommends that regulations governing the presence of chromium in drinking water distinguish between the nutritionally useful trivalent and the more toxic hexavalent form.

SUMMARY

Table 30 shows the Recommended Dietary Allowances (RDA's) for various nutrients discussed in this report. Table 31 shows estimated adequate and safe intakes for nutrients for which a RDA has not been established.

Table 32 shows the contribution that drinking water can make to the requirement for or the intake of these nutrients. These calculations are generally for the concentrations of elements in water from large water supply systems. A sizeable portion of the population (16.7%) is served by systems supplying less than 25 persons. The minerals in water from such systems may exceed the concentrations used in these calculations, but extensive information on such systems is not yet available.

TABLE 30

Recommended Dietary Allowances[a]

Group	Age, Years	Weight, kg	RDA, mg/day Calcium	Magnesium	Phosphorus	Iodine	Iron	Zinc
Infants	0.0-0.5	6	360	60	240	0.035	10	3
	0.5-1.0	9	540	70	400	0.045	15	5
Children	1-3	13	800	150	800	0.060	15	10
	4-6	20	800	200	800	0.080	10	10
	7-10	30	800	250	800	0.110	10	10
Males	11-14	44	1,200	350	1,200	0.130	18	15
	15-18	61	1,200	400	1,200	0.150	18	15
	19-22	67	800	350	800	0.140	10	15
	23-50	70	800	350	800	0.130	10	15
	51+	70	800	350	800	0.110	10	15
Females, not pregnant	11-18	44-54	1,200	300	1,200	0.115	18	15
	19-50	58	800	300	800	0.100	18	15
	51+	58	800	300	800	0.080	10	15
Females, pregnant			1,200	450	1,200	0.125	18+[b]	20
Females, lactating			1,200	450	1,200	0.150	18	25

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[a] From NAS, 1974. The allowances are intended to provide for individual variations among most normal persons as they live in the United States under usual environmental stresses. Diets should be based on a variety of common foods to provide other nutrients for which human requirements have been less well defined.

[b] This increased requirement cannot be met by ordinary diets; therefore, the use of supplemental iron is recommended.

TABLE 31

Estimated Adequate and Safe Intakes[a]

Group	Age, Years	Estimated Adequate and Safe Intakes, mg/day							
		Fluorine	Sodium	Potassium	Copper	Selenium,	Manganese	Molybdenum	Chromium
Infants	0-0.5	0.1-0.5	115-345	350-925	0.5-0.7	0.1-0.04	0.5-0.7	0.03-0.06	0.01-0.04
	0.5-1	0.2-1.0	250-750	425-1,275	0.7-1.0	0.02-0.06	0.7-1.0	0.04-0.08	0.02-0.06
Children	1-3	0.5-1.0	325-975	550-1,650	1.0-1.5	0.02-0.08	1.0-1.5	0.05-0.1	0.02-0.08
	4-6	1.0-2.5	450-1,350	775-2,350	1.5-2.0	0.03-0.12	1.5-2.0	0.06-0.15	0.03-0.12
	7-10	1.5-2.5	600-1,800	1,000-3,000	2.0-2.5	0.05-0.2	2.0-3.0	0.1-0.3	0.05-0.2
	11+	1.5-2.5	900-2,700	1,525-4,575	2.0-3.0	0.05-0.2	2.5-5.0	0.15-0.5	0.05-0.2
Adults		1.5-4.0	1,100-3,300	1,875-5,600	2.0-3.0	0.05-0.2	2.5-5.0	0.15-0.5	0.05-0.2

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[a] NAS, in press. Any daily intake within the ranges recommended in this table is considered adequate and safe. The recommendations do not imply that intakes at the upper limit of the range are more desirable or beneficial than those at the lower limit.

TABLE 32

The Contribution of U.S. Drinking Water to Mineral Nutrition of Humans

Nutrient	Body Content, mg[a]	Level in water, mg/l Typical[b]	Level in water, mg/l Maximum[c]	Requirements, mg/day[d] RDA	Requirements, mg/day[d] Adequate and Safe Intake	Requirements, mg/day[d] Calculated[e]	Typical Intake (F, Food; T, Total) mg/day	Contribution from Water, % To Requirement Typical	Contribution from Water, % To Requirement Maximum[c]	Contribution from Water, % To Intake[f] Typical	Contribution from Water, % To Intake[f] Maximum[c]	Comments
Calcium	1,000,000	26	145	800			500-1,000 (F)	6.5	36	5-10	29-58	
Magnesium	19,000	6.25	120	300-400			240-480 (F)	3-4	60-80	2.4-4.8	33-50	
Phosphorus	780,000	Undetectible	3.0	800			1,500 (F)	Negligible	Negligible	Negligible	Negligible	
Fluoride	2,600	0.4	7.0	See text[g]				See text[g]		See text[g]		
Sodium	80,000	28	220		1,100-3,300		1,600-9,600 (T)	1.7-5.0	13.3-40	0.6-3.4	4-27	Intake generally too high
Potassium	145,000	2.15	8.3		1,875-5,600		1,500-6,000 (T)	Negligible	Negligible	Negligible	Negligible	Low intake by the elderly
Chloride	95,000	21	179	No Recommendation Exists			2,400-14,000 (T)	Requirement Not Clear		0.3-2	2.5-15	
Iodine	20	0.004	0.018	0.14 ♂ 0.10 ♀			0.240-0.740 (F)	8 ♀ : 6 ♂	19-44	1-3	5-15	Intake generally high
Iron	4,000-5,000	0.240	2.20	10 ♂ 18 ♀			19.0 (F)	<3 ♀ : 5 ♂	24 ♀ : 44 ♂	2.5	23	Bioavailability important
Copper	80	0.100	0.450		2-3		1.5 (F)	6-10	30-45	12	38	
Zinc	1,400-2,300	<0.200	1.50	15			12.0 (F)	2.7	20	3.1	20	
Selenium	14.6	0.001	0.0066[i]		0.050-0.200		0.150[h]	Negligible	7-26[h]	Negligible	8[h]	MCL=0.01 mg/l
Manganese	20	0.025	1.32		2.5-5.0		1-6.4 (F)	1-2	50-100	<1-5	29-72	
Arsenic	3.5	<0.0024[i]	(MCL=0.050)[j]			0.025-0.050	0.0114 (T)	<10-19	See footnote[j]	<30	See footnote[j]	
Nickel	10.0	0.005	0.075			0.050	0.165-0.500 (F)	20	100	2-6	23-50	
Vanadium	0.10	0.004	0.070			0.025	0.02 (F)	32	100	29	Near 90	
Molybdenum	9.3	<0.002[i]	0.068		0.15-0.50		0.100 (F)	<0.8-2.7	27-91	<3.8	57	
Silicon	NRD[k]	7.1	72	No Recommendation Exists			NRD[k]	Requirement not clear		NRD[k]	NRD[k]	
Chromium	NRD[k]	0.0085	0.112 (>MCL of 0.050)		0.05-0.20		0.062 (F)	8.5-34	50-100 at MCL	22	62 at MCL	Valence form important

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[a] Values are based on a 70-kg adult. Sources are referenced in the text or data are from Masironi (1978) or the International Commission on Radiological Protection (1975).

[b] This level is considered by the committee to be a realistic assessment of a 'typical' level. It is not derived by any particular statistical method because water composition data are often reported in such a manner that it is difficult to apply such methods to them.

[c] This is the highest level observed in the studies cited in this report but should not be taken as the maximum level that might occur.

[d] The values given are for young adults. As can be seen from Tables 30 and 31, recommendations vary with age and reproductive status. RDA = Recommended Dietary Allowance (NAS, 1974). 'Adequate and Safe Intake' Values are from NAS (in press).

[e] This value was derived by extrapolating from animal studies. It was done merely for illustrative purposes and should not be taken as a recommendation.

[f] The percent contribution from water is calculated as a proportion of the total intake from both food and water.

[g] Major benefit from correct fluoride intake accrues to children. This is discussed more fully in the text.

[h] Intake varies regionally and in different countries. See section of text on selenium.

[i] The typical level is probably much lower than this value since many of the samples tested did not contain detectable levels of the element and were not included in this average.

[j] When higher concentrations were observed, e.g., 2.0 mg/l in water from some deep wells (see section on arsenic), the water was blended with water containing less arsenic in such a way that the Maximum Contaminant Level (MCL) of 0.05 mg/l was not violated. Arsenic intake from 2 l of water per day containing the MCL would be far greater than that from food.

[k] NRD = No Reliable Data.

CONCLUSIONS

At their typical levels in drinking water, the nutrients reviewed in this report usually make a small, but by no means negligible, contribution to the mineral nutrition of humans.

When the intake of a particular nutrient by the general population or a particular group is marginal, the contribution by water may be important in preventing deficiency and ill health. This may be the case for magnesium, fluoride, iron, copper, zinc, vanadium, and chromium.

For the overwhelming majority of the nutrients studied, the risk of toxicity to normal individuals from typical levels in drinking water is negligible. When the level of a nutrient in drinking water is typical and reduction of total intake is prudent (e.g., for iodine or for sodium), reduction from sources other than water would seem to be the option by which the largest initial reduction could be made.

The accurate assessment of the contribution of water to nutrition is hampered by the lack of information on the speciation and bioavailability of elements, particularly in drinking water. Additionally, water treatment practices, e.g., addition of phosphates for corrosion control, may alter nutrient composition of water, as might the use of chelators in food preparation.

RESEARCH RECOMMENDATIONS

The speciation of essential elements in drinking water and food and their respective bioavailabilities should be investigated.

Information on the mineral composition of water to be collected in the U.S. Environmental Protection Agency's National Statistical Assessment of Rural Water Conditions should be evaluated to determine if mineral levels in such waters and their contributions of water to nutrition differ greatly from those reviewed above.

A review of water treatment and distribution practices is desirable to define the ways in which such practices contribute to or alter the nutrient composition of water.

Suggested changes in water treatment practice, e.g., the introduction of granular activated carbon treatment, should be evaluated on a pilot-plant scale to determine how they would affect the nutrient composition of drinking water.

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